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(54) Title: COMPOSITIONS AND USES FOR SENTRIN, A CELL-DEATH PROTECTING PROTEIN

(57) Abstract

Disclosed are compositions comprising a novel cell-death protecting protein, sentrin-1, and the gene which encodes it. Also disclosed are methods of making and using sentrin polypeptides and nucleic acid segments in various diagnostic and pharmaceutical applications. In a preferred embodiment, overexpression of sentrin-1 confers protection against both anti-Fas/APO-1 and TNF-induced apoptosis.

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WD-40 - DERIVED PEPTIDES AND USES THEREOF

Field of the Invention

The present invention relates in general to compositions and methods of modulating the function of proteins involved in protein-protein interactions. It relates more specifically to modulating the function of a first protein of a pair of interacting proteins wherein a second protein of the pair contains a "WD-40" or "ß-transducin" amino acid repeat motif.

10 Background Art

Many intracellular processes are carried out or regulated by multi-subunit protein complexes that become active or repressed by the association or dissociation of individual polypeptide subunits.

One such group or family of proteins is related to the ß subunit of transducin. Members of this group are all at least somewhat homologous to the ß-subunit of transducin at the amino acid level, and contain a varying number of repeats of a particular motif identified in ß-transducin. The repeats have been termed "ß-transducin", or "WD-40" repeats (Fong, et al.).

Among the members of this protein family (Duronio, et al.) are the G β subunits that couple many receptors to their intracellular effector molecules, $G\beta/\gamma$ subunits that anchor another protein kinase (the β -adrenergic receptor kinase, β ARK),

25 DNA binding proteins and yeast cell cycle proteins. All of these require a transient protein-protein interaction for their function. However, the sequences at the interface of these proteins and their partners have not been identified.

The following are the references cited above and 30 throughout the specification:

U.S. Patent Documents

Crea, R., U.S. Patent No. 4,888,286, issued December 19, 1989.

Eaton, M.A.W., et al., U.S. Patent No. 4,719,180, 35 issued Jan. 12, 1988.

Yoshio, T., et al., U.S. Patent No. 4,849,350, issued July 18, 1989.

Other References

Ausubel, F. M., et al., Current Protocols in Molecular

Biology, John Wiley and Sons, Inc., Media PA.

Bohinski, R.C., Modern Concepts in Biochemistry,

Second Edition, Allyn and Bacon, Inc.

Dayhoff, M.O., in Atlas of Protein Sequence and

Structure (1972) Vol. 5, National Biomedical Research

10 Foundation, pp. 101-110, and Supplement 2 to this volume, pp. 1-10.

Duronio, R.J., et al., (1992) Proteins: Structure, Function, and Genetics 13:41-56.

Escobedo, J.A., et al., Mol. Cell. Biol., 11:1125-1132

15 (1991).

20

2166.

Fong, et al., (1986) Proc Natl Acad Sci USA 83:2162-

Hari, et al., Endocrinology, 120:829-831 (1987).

Kleuss, C., et al., Science 259:832-834 (1993).

Makowske, O.M. and Rosen, O.M. J. Biol. Chem.

264:16155-16159 (1989)

Maniatis, T., et al., <u>Molecular Cloning: A Laboratory</u>
Manual, Cold Spring Harbor Laboratory (1982).

Miller, J.F., et al., Nature (London) 216:659-63

25 (1969).

Mochly-Rosen, D., and Koshland, D. E., Jr. J. Biol. Them. 262:2291-2297 (1987).

Mochly-Rosen, et al., Molec. Biol. Cell. 1:693-706 (1990).

30 Mochly-Rosen, D., et al., Proc. Natl. Acad. Sci. USA 88:3997-4000 (1991).

Orr, J.W., et al., J. Biol. Chem. 267, 16155-16159 (1992)

Pitcher, J., et al., Science 257:1264-1267 (1992).

35 Reiner, et al., Nature 364:717-721 (1993).

Schulz, G.E. and R.H. Schirmer., <u>Principles of Protein</u>
<u>Structure</u>, Springer-Verlag.

Smith, B.L. and Mochly-Rosen, D. Biochem. Biophys. Res. Commun. 188:1235-1240 (1992).

Smith, D.B., et al., Gene 67:31 (1988).

Stith, B.J. and J.L. Maller. Exp. Cell. Res. 169:514-5 523 (1987).

Wolf, M. and N. Sahyoun, Chem., 261:13327-13332 (1986).

Disclosure of the Invention

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The invention includes, in one aspect, a polypeptide composition effective to alter the activity of a first protein, such as protein kinase C, or β -adrenergic receptor kinase (β ARK). The polypeptide blocks or inhibits an interaction, such as a binding interaction, between the first protein and a second protein containing a WD-40 region.

The polypeptide contains between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

The polypeptide may block the binding of the first to the second protein, or may be an agonist or antagonist of the 20 first protein. The WD-40 region preferably has an amino acid sequence homologous or identical to the sequences defined by SEQ ID NO:76-261.

In a second embodiment, the invention includes a method of altering the activity of the first protein of the type defined above. The method includes selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein, and contacting the polypeptide with the first protein under conditions which allow the formation of a complex between the polypeptide and the first protein, where this interaction alters the activity of the first protein.

In one embodiment, the contacting is effective to inhibit the interaction between the first and second proteins.

In another embodiment, the contacting is effective to stimulate the activity of the first protein.

In still another embodiment, the contacting is effective to inhibit the activity of the first protein.

- 4 -

The polypeptide preferably has an amino acid sequence homologous or identical to the sequences defined by SEQ ID NO:76-261.

In a more specific aspect of the invention, the

invention includes a polypeptide composition effective to alter
the activity of protein kinase C, where the protein kinase C
interacts with a second protein, and the second protein contains
at least one WD-40 region. The polypeptide has between 4 and 50
amino acids whose sequence is the same as a sequence of the same
length in the WD-40 region of the second protein.

In a preferred embodiment, the second protein is a receptor for activated protein kinase C, and has the sequence represented by SEQ ID NO:27.

In other specific embodiments, the polypeptide is (i)

an agonist of protein kinase C, and the polypeptide has the sequence represented by SEQ ID NO:7; (ii) an antagonist of the activity of protein kinase C; and/or (iii) an inhibitor of the interaction between protein kinase C and the second protein. In the latter embodiment, the polypeptide has sequence corresponding to SEQ ID NO:4 or SEQ ID NO:7.

The WD-40 region preferably has an amino acid sequence homologous or identical to SEQ ID NO:69-75.

In a related embodiment, the invention includes a method of altering the activity of a protein kinase C that interacts with a second protein, where said second protein contains at least one WD-40 region.

The method includes selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein, and contacting the polypeptide with the protein kinase C under conditions which allow the formation of a complex between the polypeptide and the protein kinase C, where said interaction alters the activity of said protein kinase C.

Other aspects of the invention include the polypeptide
compositions of the invention wherein said polypeptide is
coupled to a solid support, as well as a method to bind
selectively said first protein which method comprises contacting
a sample putatively containing said first protein with the

WO 95/21252

- 5 -

polypeptide composition bound to solid support and removing any unbound components of the sample from said composition.

In still another aspect, the invention relates to a method to assess the interaction of a first protein with a 5 polypeptide represented by an amino acid sequence contained in a second protein, wherein said second protein contains at least one WD-40 region, which method comprises contacting a sample containing said first protein with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose 10 sequence is the same as the sequence of the same length in the WD-40 region of the second protein, and observing any interaction of the first protein with said polypeptide The invention also concerns a method to assess the ability of a candidate compound to bind a first protein which 15 method comprises contacting said first protein with a polypeptide composition which binds said first protein, wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts 20 with said first protein, in the presence and absence of said candidate compound; and measuring the binding of said polypeptide in the presence and in the absence of said candidate, wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates 25 that said candidate binds to said first protein.

In still another aspect, the invention is directed to recombinant materials for the production of the polypeptides of the invention and methods for their production.

These and other objects and features of the invention 30 will become more fully apparent when the following detailed description of the invention is read in conjunction with the accompanying drawings.

Brief Description of the Figures

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Figure 1A shows the cDNA sequence of rat brain RACK1. Figure 1B shows an amino acid self-homology matrix analysis of RACK1.

PCT/US95/01210

WO 95/21252

- 6 -

Figure 1C shows the amino acid sequence of RACK1,

aligned to show the seven WD-40 repeats represented in the molecule.

Figure 2 shows the results of an overlay assay to 5 detect PKC binding to immobilized RACK1 in the presence and absence of PKC activators.

Figure 3 shows the results of an overlay assay to detect PKC binding to immobilized RACK1 in the presence and absence of WD-40-derived peptides.

Figure 4 shows the results of an overlay assay to 10 detect binding of β PKC to either peptide I (SEQ ID NO:1) or peptide rVI (SEQ ID NO:7) immobilized on nitrocellulose membranes under various conditions.

Figure 5A shows the effects of injecting peptides I (SEQ ID NO:1) and rVI (SEQ ID NO:7) on PKC-mediated germinal 15 vesicle breakdown (GVBD), a measure of insulin-induced oocyte maturation.

Figure 5B shows the effects of injecting peptides I (SEQ ID NO:1) and rVI (SEQ ID NO:7) on PKC-mediated germinal 20 vesicle breakdown (GVBD) in the absence of insulin induction.

Figure 5C shows the effects of injecting peptide rIII (SEQ ID NO:4) on PKC-mediated germinal vesicle breakdown (GVBD) in the absence of insulin induction.

Figure 6 shows the distribution of β PKC in Xenopus oocytes between the cytosolic and membrane-associated fractions following microinjection of either injection solution, peptide I (SEQ ID NO:1) or peptide rVI (SEQ ID NO:7) with or without insulin stimulation.

Figure 7 shows the effects of peptides I and rVI on 30 the sensitivity of β PKC to Arg-C endopeptidase.

Figure 8 shows the effects of peptides I and rVI on PKC autophosphorylation in the absence of PKC activators.

Figure 9 shows the effects of peptides I and rVI on PKC phosphorylation of histones in the absence of PKC activators.

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Figure 10 shows the effects of peptide rIII on PKC phosphorylation of histones in the absence of PKC activators.

- 7 -

Figure 11 shows the amino acid sequence of the 56 kDa human protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 12 shows the amino acid sequence of the AAC-5 rich protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 13 shows the amino acid sequence of the B-TRCP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 14 shows the amino acid sequence of the Betaprime-COP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

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Figure 15 shows the amino acid sequence of the CDC4 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 16 shows the amino acid sequence of the Chlam-3 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 17 shows the amino acid sequence of the COP-20 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 18 shows the amino acid sequence of the CORO protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 19 shows the amino acid sequence of the Coronin p55 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 20 shows the amino acid sequence of the Cstf 50 kDa protein with the WD-40 repeats aligned and putative binding 30 peptide regions delineated by a box.

Figure 21 shows the amino acid sequence of the bovine G-beta-1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 22 shows the amino acid sequence of the bovine 35 G-beta-2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

- 8 -

Figure 23 shows the amino acid sequence of the drosophila G-beta protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 24 shows the amino acid sequence of the human 5 G-beta-1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 25 shows the amino acid sequence of the human G-beta-2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 26 shows the amino acid sequence of the mouse G-beta protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

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Figure 27 shows the amino acid sequence of the drosophila groucho protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 28 shows the amino acid sequence of the squid GTP-binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 29 shows the amino acid sequence of the HSIEF 20 930 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 30 shows the amino acid sequence of the human 12.3 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 31 shows the amino acid sequence of the human IEF-7442 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 32 shows the amino acid sequence of the insulin-like growth factor binding protein complex with the WD-30 40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 33 shows the amino acid sequence of the rat insulin-like growth factor binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 34 shows the amino acid sequence of the human LIS1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

PCT/US95/01210

- 9 -

Figure 35 shows the amino acid sequence of the MD6 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

WO 95/21252

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Figure 36 shows the amino acid sequence of the yeast 5 MSI1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 37 shows the amino acid sequence of the mouse pc326 MUS protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 38 shows the amino acid sequence of the ORD RB1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 39 shows the amino acid sequence of the periodic trp protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 40 shows the amino acid sequence of the PLAP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 41 shows the amino acid sequence of the retinoblastoma binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 42 shows the amino acid sequence of the S253 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 43 shows the amino acid sequence of the SOF1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 44 shows the amino acid sequence of the STE4 yeast protein with the WD-40 repeats aligned and putative 30 binding peptide regions delineated by a box.

Figure 45 shows the amino acid sequence of the TF1 transcription factor protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 46 shows the amino acid sequence of the TUP1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 47 shows the amino acid sequence of the TUP1 homolog protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 48 shows the amino acid sequence of the YCU7 5 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 49 shows the amino acid sequence of the YCW2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 50 shows the amino acid sequence of the YKL25 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 51 shows the amino acid sequence of the YRB140 protein with the WD-40 repeats aligned and putative binding 15 peptide regions delineated by a box.

Detailed Description of the Invention

I. <u>Definitions</u>

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Unless otherwise indicated, all terms used herein have the same meaning as they would to one skilled in the art of the 20 present invention. Practitioners are particularly directed to Current Protocols in Molecular Biology (Ausubel) for definitions and terms of the art.

Abbreviations for amino acid residues are the standard 3-letter and/or 1-letter codes used in the art to refer to one 25 of the 20 common L-amino acids. Likewise, abbreviations for nucleic acids are the standard codes used in the art.

An "amino acid group" refers to a group of amino acids where the group is based on common properties, such as hydrophobicity, charge, or size.

A "conserved set" of amino acids refers to a contiguous sequence of amino acids that is conserved between members of a group of proteins. A conserved set may be anywhere from two to over 50 amino acid residues in length. Typically, a conserved set is between two and ten contiguous residues in length. The individual positions within a conserved set each typically comprise one of several amino acids, selected from an

amino acid group(s). In cases where a residue is 100% conserved

PCT/US95/01210 WO 95/21252

- 11 -

at a particular position, the conserved set sequence will contain only that residue at that position. For example, for the two peptides WRTAA (SEQ ID NO:263) and WRTAV (SEQ ID NO:264), there are 4 identical positions (WRTA; SEQ ID NO:265) and one position where the residue is an "A" or a "V".

Proteins are typically long chains of amino acid based polyamides (polypeptides) capable of creating secondary and tertiary structure. Proteins may be composed of one, two or more polypeptide chains and may further contain some other type 10 of substance in association with the polypeptide chain(s), such as metal ions or carbohydrates. The size of proteins covers a rather wide range from ~5,000 to several hundred thousand g/mole. The 5,000 figure corresponds to the presence or roughly 40-45 amino acids.

15 Unless otherwise indicated, the sequence for proteins and peptides is given in the order from the amino terminus to the carboxyl terminus. Similarly, the sequence for nucleic acids is given in the order from the 5' end to the 3' end.

The term "interacting proteins" refers to a pair of 20 polypeptides that can form a stably-associated complex due to, for example, electrostatic, hydrophobic, ionic and/or hydrogenbond interactions under physiological conditions.

Proteins smaller than about 5,000 g/mole are typically referred to as polypeptides or simply peptides (Bohinski).

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Two amino acid sequences or two nucleotide sequences are considered homologous (as this term is preferably used in this specification) if they have an alignment score of >5 (in standard deviation units) using the program ALIGN with the mutation gap matrix and a gap penalty of 6 or greater (Dayhoff). 30 The two sequences (or parts thereof) are more preferably homologous if their amino acids are greater than or equal to 50%, more preferably 70%, still more preferably 80%, identical

A peptide or peptide fragment is "derived from" a 35 parent peptide or polypeptide if it has an amino acid sequence that is identical or homologous to the amino acid sequence of the parent peptide or polypeptide. Homologous peptides are defined above. Exemplary derived peptides are peptide rIII (SEQ

when optimally aligned using the ALIGN program mentioned above.

PCT/US95/01210

WO 95/21252

- 12 -

ID NO:4) and peptide rVI (SEQ ID NO:7), which are derived from the third and seventh WD-40 repeats of RACK1 (SEQ ID NO:27), respectively.

The term "expression vector" refers to vectors that 5 have the ability to incorporate and express heterologous DNA fragments in a foreign cell. Many prokaryotic and eukaryotic expression vectors are commercially available. Selection of appropriate expression vectors is within the knowledge of those having skill in the art.

The term "PKC" refers to protein kinase C, or C-10 kinase.

The term "RACK" refers to receptor for activated Ckinase.

The term "PS" refers to phosphatidylserine.

The term "DG" refers to diacylglycerol.

The term "PL" refers to phospholipids. Phospholipids include both phosphatidylserine and diacylglycerol.

The term "GVBD" refers to germinal vesicle breakdown, a measure of insulin-induced maturation in Xenopus oocytes.

The term "PCR" refers to polymerase chain reaction.

The term "NMR" refers to nuclear magnetic resonance.

The term " β ARK" refers to β -adrenergic receptor kinase.

General Overview of Invention.

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The invention relates to interacting proteins, at 25 least one of which contains an amino acid sequence with one or more of the characteristic repeats termed WD-40 (Fong, et al.).

According to one aspect of the invention, the function of a first protein of a pair of interacting proteins may be 30 modulated, altered or disrupted by the addition, to a solution or medium containing the protein, of a peptide having a sequence that is identical or homologous to a part of the sequence of a WD-40 motif-containing repeat present in a second protein of the pair of interacting proteins.

The modulation or disruption of function of the first protein is due to the binding or association of the WD-40derived peptide, termed "binding peptide", with the first

- 13 -

protein. The consequences of the binding or association of the binding peptide with the first protein depend on the sequence of the peptide.

Typically, the presence of the binding peptide will inhibit the binding of the first protein to the second protein. This binding may be assayed in vitro by, for example, an overlay assay, whereby the degree of binding of one protein to another may be assessed. Several adaptations of overlay assays applied to embodiments of the present invention are described herein.

Regardless of whether or not the WD-40-derived peptide affects the association of the first protein with the second protein, the peptide may alter or modulate defined activities of the first protein. These activities may be assayed by a variety of methods in vivo and/or in vitro. The method(s) employed depend on the protein whose activity is being measured.

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An exemplary first protein of a pair of interacting proteins is protein kinase C (PKC). Upon activation, PKC interacts with receptors for activated C kinase (RACKs), at least one of which (RACK1) contains WD-40 repeats. Several assays for determining the activity of PKC in the presence and in the absence of peptides derived from the WD-40 region of RACK1 are detailed herein.

Certain "interacting proteins" interact only after one or more of them has been stimulated by an exogenous or endogenous factor(s). For instance, PKC, as shown herein, does not bind to RACK proteins until it has been activated by, for example, phosphatydilserine (PS), diacylglycerol (DG) and calcium. However, peptides derived from WD-40 repeats of a second protein of such a pair may be able to associate with or bind to the first protein even in the absence of activators of the first protein, and in so doing, affect the function of the first protein (e.g. activate, inactivate, potentiate, sensitize, desensitize, alter the specificity, etc.).

Binding peptides derived from WD-40 repeats of a

35 second protein of a pair of interacting proteins, may be useful
as specific agonists, antagonists, potentiators of function, and
the like, of the first protein of the pair. These properties
may make the peptides useful in a number of applications, for

example, direct use in therapeutic applications or as lead compounds for the development of other therapeutic agents, e.g., small organic molecules.

III. Advantages of the Invention for the Inhibition of Activated PKC Binding to RACK1.

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Protein kinase C (PKC) is a family of at least 10 isozymes that share common structures and biochemical characteristics. It has been demonstrated that several isozymes are present within a single cell type, and it has been assumed 10 that individual PKC isozymes are involved in different cellular functions. However, so far, the available activators and inhibitors of PKC do not appear to be isozyme-specific. Therefore, it is currently impossible to determine the role of individual PKC isozymes in normal cellular functions as well as in disease.

PKC activation by, for example, diacylglycerol and calcium, induces the translocation of PKC from a soluble (cytosolic) to a cell particulate (membrane-associated) fraction, as shown in experiments herein (Example 8). Activated 20 PKC is stabilized in the cell particulate fraction by binding to membrane-associated receptors (receptors for activated C-Kinase, or RACKs).

In experiments done in support of the present invention and described herein, a clone (pRACK1) encoding a RACK 25 has been isolated (Example 1). RACK1 belongs to a growing family of proteins that are homologous to the ß-subunit of transducin and contain the WD-40 motif (Fong, et al.). demonstrated that peptide I (SEQ ID NO:1) binds to purified PKC (see Example 6 and Fig. 4), inhibits the binding of PKC to 30 purified recombinant RACK1 protein (see Example 4 and Fig. 3), and inhibits PKC activity in several in vivo and in vitro assays (see Examples 7-11 and Figs. 5-9).

Peptide I (SEQ ID NO:1) is homologous to a sequence identified in the sixth WD-40 repeats of RACK1 (see Fig. 1C). A 35 synthetic peptide was prepared based on this sequence (peptide rVI; SEQ ID NO:7; underlined amino acids in repeat VI of Fig. 1C). Six more peptides were also prepared based on the

- 15 -

corresponding regions in repeats I-V and VII (peptides rI-rV, rVII; SEQ ID NO:2-6, 8; underlined regions in corresponding repeats, Fig. 1C). Some of the peptides were also found to inhibit the binding of PKC to RACK1 (see Example 4 and Fig. 3). In addition, some of the peptides were found to bind to purified PKC (see Example 6, Fig. 4), partially activate PKC in the absence of other activators (peptide rVI; see Examples 7, 10, 11 and Figs. 5, 8 and 9), and potentiate the effects of known PKC

In Xenopus oocyte maturation studies (see, for instance, Example 7), peptide rVI (SEQ ID NO:7) is an agonist of βPKC. Peptide rIII, while less potent, is also an agonist of PKC; it enhances insulin-induced oocyte maturation at 50 and 500μM.

activators on the enzyme (see Examples 7-9 and Figs. 5-7).

In cardiac myocytes, norepinephrine (NE, 2μM) causes translocation of δ and εPKC isozymes from the cytosolic to the particulate fraction. Introduction into cardiac myocytes of peptide rIII, and to a lesser extent peptide rVI, caused an immediate translocation of δ and εPKC isozymes in the absence of hormone stimulation. This peptide-induced translocation was followed by degradation of δ and εPKC isozymes. Moreover, NE-induced translocation is further enhanced in cells containing peptide rIII.

In contrast, introduction of peptide I to these cells does not affect PKC distribution in the absence of hormone stimulation, nor does it induce PKC degradation. Furthermore, NE-induced translocation is inhibited by peptide I. Similar concentrations of a number of control peptides did not affect PKC distribution or degradation in control or NE-treated cells.

In studies on rat cardiac myocytes, peptide rIII induced δ PKC and ϵ PKC activation that was followed by degradation of these activated isozymes.

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Peptide rVI also augments hormone-induced translocation of PKC isozymes (see, for example, Example 8 and Fig. 6). In contrast, peptide I (SEQ ID NO:1) inhibited hormone-induced translocation of PKC isozymes (Example 8, Fig 6) and did not cause degradation.

WO 95/21252

- 16 -

The data summarized above demonstrate that peptides derived from WD-40 repeats of RACK1 can serve as PKC agonists and antagonists in vivo, and suggest that peptides derived from WD-40 regions of RACK1 contain at least part of the protein-5 protein interface between PKC and RACK1.

Furthermore, the results suggest that (i) WD-40 repeats present in other proteins, such as $G\beta$ subunit, may also be located at or near a surface involved in protein-protein interactions, (ii) peptides derived from these repeats may be 10 effective in disrupting the interactions of the proteins with their partners (e.g. β -adrenergic receptor kinase (β ARK), (iii) the peptides may modulate or alter the activity of the proteins with which the WD-40 repeat-containing proteins interact, and (iv) the peptides may therefore have specific biological effects when administered in vivo.

Identification of Pairs of Interacting Proteins. IV.

Biochemical Approaches. Α.

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Novel interacting proteins may be identified and isolated by a number of methods known to those skilled in the art. For example, monoclonal antibodies raised to a mixture of antigens, such as a particular tissue homogenate, may be characterized and used to immunoprecipitate a single class of antigen molecules present in that tissue. The precipitated proteins may then be characterized further, and used to co-25 precipitate other proteins with which they normally interact (Hari, et al., Escobedo, et al.).

An alternate method to identify unknown polypeptides that interact with a known, isolated protein is by the use of, for example, an overlay assay (Wolf, et al., Mochly-Rosen, et 30 al., 1991). A mixture (such as a fraction of a tissue homogenate, for example, a Triton-insoluble protein fraction) potentially containing proteins that bind to a known, isolated protein can be resolved using PAGE, blotted onto a nitrocellulose or nylon membrane, and contacted with a solution 35 containing the known protein and any necessary co-factors or small molecules. After washing, the membrane can be contacted

- 17 -

with a probe for the known protein, for example an antibody or a mixture of antibodies, and the signal visualized.

B. Molecular Approaches.

Putative binding proteins of a known protein may be
isolated from tissue homogenates, as described above.
Alternatively, DNA clones encoding putative binding proteins may
be identified by screening, for example, an appropriate cDNA
expression library. Expression libraries made from a wide
variety of tissues are commercially available (for example, from
Clonetech, Palo Alto, CA). Expression libraries may also be
made de novo from organisms and tissues of choice by
practitioners skilled in the art.

The screening of expression libraries for clones expressing a protein or protein fragment of interest may be readily accomplished using techniques known in the art, for example, an overlay assay.

An overlay-assay screening method may be used to identify clones expressing a (known or unknown) protein or protein fragment that binds to a probe in hand. The probe may 20 be a protein postulated to be involved in protein-protein interactions with a protein expected to be present in a cDNA library selected for screening (as was the case for the cloning of RACK1, detailed in Example 1).

accomplished by inducing plated clones to express cloned exogenous sequences, transferring replicas of the induced plaques or colonies to filter membranes, and screening the membranes with an appropriate probe. According to this method, lifts of filters (for example, nylon or nitrocellulose) from an appropriately-induced cDNA library plates (induced by, for example, IPTG) are washed, blocked, and incubated with a selected probe for a period of time sufficient to allow the selected probe(s) to bind specifically to polypeptide fragments present on the filters. The filters may then be washed and reacted with a reagent (for example, antibodies such as alkaline phosphatase-conjugated goat anti-rabbit or anti-mouse antibodies, available from Boehringer Mannheim Biochemicals,

Indianapolis, IN). Additional reactions may be carried out as required to detect the presence of bound probe.

One such overlay assay, described in Example 1, was used to screen a rat brain cDNA expression library for proteins that bind purified PKC in the presence of PKC activators (phosphatydilserine, diacylglycerol and calcium). The filters were screened with a mixture of rat brain PKC isozymes (α , β , γ , δ , ϵ and ζ). Following a series of washes, bound PKC isozymes were detected with a mixture of anti- α , β , γ PKC mouse 10 monoclonal antibodies, and anti- δ , ϵ and ζ PKC rabbit polyclonal antibodies. Bound antibodies were detected using alkaline phosphatase-conjugated goat anti-rabbit or anti-mouse antibodies and 5-bromo-4-chloro-3-indoyl phosphate p-toluidine salt as a substrate.

Once a clone is identified in a screen such as the one described above, it can be isolated or plaque purified and sequenced. The insert may then be used in other cloning reactions, for example, cloning into an expression vector that enables efficient production of recombinant fusion protein.

Examples of appropriate expression vectors are pGEX (Smith, et al., 1988) and pMAL-c2 (New England BioLabs, Beverly, MA). An expression vector containing an insert of interest may be used to transform appropriate host cells, such as E. coli, and the transformed host cells can be used to produce the recombinant protein in large amounts.

Typically, a recombinant protein is expressed in tandem with a bacterial or viral gene product (endogenous polypeptide) as part of a fusion protein. The junction between the endogenous polypeptide and the recombinant protein typically includes a recognition site for a rare-cutting protease. The endogenous peptide may be designed to incorporate a unique affinity tag (a short peptide sequence) to facilitate the purification of the fusion protein with an affinity reagent, such an antibody directed against the affinity tag. The recombinant protein may then be purified from the fusion protein using the appropriate protease.

Purified recombinant protein may be used in a number of ways, including in an overlay binding assay to screen for

peptides or substances that inhibit binding between the recombinant protein and an interacting protein.

An example of the use of a cDNA clone to express protein is detailed in Example 2. RACK1 cDNA, isolated as

5 described above and in Example 1, was subcloned into an expression vector (pMAL-c2, New England BioLabs, Beverly, MA) capable of expressing a cloned insert in tandem with maltose-binding protein (MBP). The vector containing the RACK1 insert was used to transform TB1 E. coli, which were then induced with

10 IPTG. The cells produced a 78 kDa fusion protein comprised of RACK1 fused to the MBP. The overexpressed fusion protein was purified on an amylose affinity column according to the manufacture's protocol (New England BioLabs, Beverly, MA) and incubated with protease Xa to separate the expressed insert from the MBP. Following the incubation, a 36 kDa RACK1 protein was obtained.

V. <u>Identification of WD-40 Repeats</u>.

According to a method of the present invention, protein-protein interactions can be disrupted and/or the activity of an interacting protein can be altered, given at least one of the interacting proteins contains a WD-40 motif, or region, with a peptide(s) derived from a WD-40 repeat(s) of one of the proteins.

WD-40 repeats are typically found in a family of
proteins having at least a limited homology with the ß subunit
of transducin. WD-40 repeats present in a selected member of
this family can be identified by (A) performing a self-homology
analysis on a selected protein using a homology matrix
(performed by, for example, the computer program DNA Strider
1.2, available from Christian Marck, Service de Biochemie et de
Genetique Moleculaire, Department de Biologie Cellulaire et
Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE),
(B) aligning sequences comprising the repeating elements
revealed by the homology matrix analysis, and (C) identifying
conserved amino acid residues that typically serve to define a
WD-40 repeat. The steps are discussed individually, below.

- 20 -

A. Homology matrix analysis.

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Determining whether a particular amino acid sequence contains repeated motifs may be accomplished by a number of methods known to those skilled in the art. They range from a simple visual inspection of the sequence to the use of computer programs which can identify repeated motifs. One widely-implemented computer-assisted method is to generate a self-homology matrix. A self-homology matrix computes the homology of each amino acid residue in a particular sequence with every other residue in that sequence. The homology scores are stored in a 2-dimensional matrix.

Values higher than a selected criterion level are flagged and displayed as points on an x-y coordinate. The x- and y-axes correspond to consecutive amino acid positions in the sequence.

An example of a self-homology matrix analysis is shown in Figure 1B. The matrix was generated using the computer program DNA Strider 1.2 (Christian Marck, Service de Biochemie et de Genetique Moleculaire, Department de Biologie Cellulaire 20 et Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE) with the amino acid sequence of RACK1 (SEQ ID NO:27) with a window setting of 21 and a stringency of 6. Some typical features of a self-homology matrix are evident in the figure. The graph shows a "primary" diagonal line extending from the 25 origin with a slope of unity, corresponding to the fact that the sequence is identical to itself. If the sequence contains repeating elements, as RACK1 does, there will be other, shorter sets of contiguous points arranged in diagonal lines substantially parallel to the primary diagonal and offset from 30 the primary diagonal in the x- or y-directions. These shorter lines identify the locations of repeating elements with the sequence. Each repeating element will result in two sets of displayed points, symmetrically distributed about the primary diagonal.

35 The data displayed in a homology matrix analysis can be used to locate and roughly align the sequences of repeating elements for a more detailed analysis. The horizontal band delineating the region between ~100 and ~130 on the y-axis in

Fig. 1B highlights the fact that portions of that region of RACKI, that is, the amino acids between about amino acid 100 and amino acid 130, are repeated a total of seven times in the sequence of RACK1. Arrows point to the repeats in the homology 5 matrix. For purposes of rough alignment, the short diagonal lines pointed out by the arrows can be extended to the horizontal line at amino acid ~100 on the y-axis, and the x-axis location corresponding to the intersection be noted. For example, the intersection corresponding to the second repeat 10 (second arrow from the left) is at x=-50).

Values determined in this manner may then be used to align the amino acid sequence of the repeats with each consecutive repeat beneath the preceding one, the start of each repeat corresponding approximately to the amino acid position 15 determined by the analysis in the preceding paragraph. The amino acid sequence of RACK1, aligned in this manner, is shown in Fig. 1C.

Most commercially-available DNA and protein sequence analysis programs have the capability to perform a self-homology 20 matrix analysis. One example is the program DNA Strider 1.2 (Christian Marck, Service de Biochemie et de Genetique Moleculaire, Department de Biologie Cellulaire et Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE).

Once the repeating elements are identified and the 25 sequences corresponding to repeating elements are roughly aligned, one may proceed to define the degree of homology among the individual repeats at the specific positions within the repeats, as is described below.

Aligning amino acid sequences. B.

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If a self-homology matrix was used to obtain a crude alignment, the sequences may aligned by eye on a personal computer or the like using, for example, a text editor, a drawing program or a sequence-analysis program. Examples of programs effective to accomplish an alignment include "MACDRAW 35 PRO" (Claris Corp., Santa Clara, CA) and "WORD" (Microsoft Corp., Redmond, WA), both of which are available for "MACINTOSH" series computers (Apple Computer Corporation, Cupertino, CA), as . - 22 -

well as IBM-compatible computers running "WINDOWS" (Microsoft Corp.).

Amino acid sequences corresponding to internal repeats can also be aligned automatically using a protein sequence 5 analysis program, such as "MACVECTOR" (Eastman Kodak Co., New Haven, CT).

According to a method of the invention, aligned sequences are examined further to determine if they fulfil criteria to be defined as WD-40 repeats. These criteria are 10 detailed in part C, below.

Amino acid residues that define a WD-40 repeat. C.

Upon completion of steps outlined in parts A and B above, that is, determining whether a particular protein contains internal repeats, and if so, aligning those repeats, it 15 is necessary to determine whether the aligned repeats contain WD-40 regions.

A WD-40 motif is roughly defined as a contiguous sequence of about 25 to 50 amino acids with relatively-well conserved sets of amino acids at the two ends (amino- and carboxylterminal) of the sequence. Conserved sets of at least one WD-40 repeat of a WD-40 repeat-containing protein typically contain conserved amino acids at certain positions. The amino-terminal set, comprised of two contiguous amino acids, often contains a Gly followed by a His. The carboxyl-terminal set, comprised of 25 six to eight contiquous amino acids, typically contains an Asp at its first position, and a Trp followed by an Asp at its last two positions.

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A more accurate definition of a WD-40 motif incorporates the observation that while specific residues, such as those identified above, are not always conserved within a WD-40 motif, conserved positions within the motif are typically occupied by residues selected from a restricted class of amino acids.

In order to better define the class of conserved 35 residues at selected positions, it is necessary to group amino acids on the basis of certain common properties. A functional way to define common properties between individual amino acids WO 95/21252

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- 23 -

is to analyze the normalized frequencies of amino acid changes between corresponding proteins of homologous organisms (Schulz). According to such analyses, groups of amino acids may be defined where amino acids within a group exchange preferentially with each other, and therefore resemble each other most in their impact on the overall protein structure (Schulz). Examples of amino acid groups defined in this manner, some of which are used in the definition of a WD-40 motif herein, include:

- (i) a charged group, consisting of Glu and Asp, Lys, Arg and His,
 - (ii) a positively-charged group, consisting of Lys, Arg and His,
 - (iii) a negatively-charged group, consisting of Glu and Asp,
 - (iv) an aromatic group, consisting of Phe, Tyr and Trp,
 - (v) a nitrogen ring group, consisting of His and Trp,
 - (vi) a large aliphatic nonpolar group, consisting of Val, Leu and Ile,
 - (vii) a slightly-polar group, consisting of Met and Cys,
 (viii) a small-residue group, consisting of Ser, Thr, Asp,
 Asn, Gly, Ala, Glu, Gln and Pro,
 - (ix) an aliphatic group consisting of Val, Leu, Ile, Met and Cys, and
 - (x) a small hydroxyl group consisting of Ser and Thr.

In addition to the groups presented above, each amino acid residue may form its own group, and the group formed by an individual amino acid may be referred to simply by the one and/or three letter abbreviation for that amino acid commonly used in the art.

A "WD-40" motif is defined herein as a contiguous set of amino acids between (inclusive) two sets of relatively well conserved residues, termed herein as an "amino-terminal set" and a "carboxyl-terminal set".

The amino-terminal set contains two adjacent amino acids. The residue at the first position is typically selected from groups ii, vi or viii, while the residue at the second position is typically selected from groups i, x or Ile. The first and second positions will often consist of Gly and His,

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respectively. The Gly and His residues are typically present in at least one of the aligned repeats of a WD-40-containing protein.

The carboxyl-terminal conserved set typically includes 5 eight residues, but may contain as few as six residues. most well-conserved residue in WD-40 motifs identified thus far is an Asp residue, comprising the first amino acid of the carboxyl-terminal conserved set. It is present in virtually all WD-40 repeats illustrated herein. In those repeats where it is 10 not present, the position is occupied by a residue from groups iii or Gly.

The last two amino acids in the carboxyl-terminal conserved set are typically selected from groups iv or Ile, and groups i or viii, respectively. The most commonly used residue 15 at the first of these positions is Trp. It is typically present in at least one of the WD-40 repeats of any given protein. The second position is occupied less consistently by a single residue, but is often occupied by Asp. The Trp-Asp (WD) combination is part of the namesake of WD-40 repeats.

The amino acids present in the internal portion of the carboxyl-terminal conserved set are less well-conserved than the terminal residues, and their total number may differ by up to two residues in different WD-40 repeats. The third position in from the carboxyl-terminal end of the carboxyl-terminal 25 conserved set is typically selected from groups viii or ix, more typically ix. The fifth position in from the carboxyl-terminal end of the carboxyl-terminal conserved set is also typically selected from groups viii or ix, more typically ix.

The length of a WD-40 repeat, including the amino-30 terminal and carboxyl-terminal conserved sets is typically between about 25 and about 50 residues, more typically between about 29 and 34 residues. The distribution arises primarily from differences in the number of residues present between the amino-terminal and carboxyl-terminal conserved sets.

The number of WD-40 repeats in a particular protein can range from two to more than eight. The average number is about 5.

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A determination of whether or not a set of aligned internal repeats are WD-40 repeats can be facilitated by an examination of all of the repeats as a whole, rather than an examination of each repeat individually. This is in part because not all of the aligned repeats will necessarily contain all of the conserved sequences that serve to identify WD-40 repeats, although the conserved residues will typically appear in at least one of the repeats.

For example, Fig. 1C shows the RACK1 amino acid

sequence aligned to illustrate the internal repeats present in
the sequence. All of the repeats are WD-40 repeats, even though
the amino-terminal conserved set of repeat VI, for instance,
contains an "LD" as opposed to the more usual "GH", and the
carboxyl-terminal conserved set contains a "G" at its first

position, as opposed to the highly-conserved "D". Similarly,
the carboxyl-conserved set of, for example, repeat I, contains a
"WK" at the last to positions, as opposed to the more usual
"WD".

of residues will be well-conserved in the WD-40 repeats of a selected protein, even though they may not be conserved in WD-40 repeats in general. Such residues or sets of residues may be useful in several ways. For example, they may be used in performing an alignment of internal repeats in a selected protein, as described in part B, above. The residues may also be useful for identifying regions based on which effective binding peptides may be designed (see section VI., below).

D. <u>Identification of WD-40 repeats in RACK1</u>.

In experiments done in support of the present
invention, a protein that binds to activated PKC was cloned and
sequenced (see Example 1). Sequence analysis of the deduced
amino acid sequence revealed the presence of repeats, which were
aligned and are shown in Figure 1C.

The aligned repeats were identified as WD-40 repeats

35 by application of the criteria identified in parts A, B and C
above. For example, the conserved amino-terminal set in repeats

I, II, III and V consists of the typical "GH", whereas in

repeats IV, VI and VII, the set consists of other residues. These other residues, however, are contained in at least one of the amino acid groups identified above as conserved at the appropriate position. The conserved carboxyl-terminal set 5 contains the highly-conserved "D" at its first position in all repeats except repeat VI. The second-to-last position of this set contains the relatively-well conserved "W" in each repeat, while the last position contains the typical "D" in repeats II, V and VI, and other residues in the other repeats.

Taken together, these data indicate that the repeats contained in RACK1 are WD-40 repeats. The data also illustrate that not all repeats contain all of the elements typical of a WD-40 motif, but that when the repeats are aligned and viewed together as a whole, a WD-40 motif is apparent in all repeats.

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Data were compiled in support of the present invention to illustrate how WD-40 repeats in various proteins may be identified, and to illustrate the diversity of amino acid sequences that may be properly identified as WD-40 repeats by

Identification of WD-40 repeats in sequenced proteins.

20 those skilled in the art following the guidance set forth herein. Two methods that were used to identify WD-40-containing protein sequences are detailed in Example 7.

In the first method, proteins identified in their description as having a homology to β -transducin were examined 25 as detailed in parts B-D, above, for WD-40 repeats. 30 proteins were identified in this manner. The amino acid sequences of these proteins, with the WD-40 regions aligned and delineated, are shown in Figs. 12-18, 20-27, 29-30, 34-35, 37-38, 40 and 42-The sequences are represented in the Sequence Listing as SEQ ID NO:29-35, 37-44, 46-47, 51-52, 54-55, 57 and 59-67.

In the second method, proteins whose sequences were homologous to a consensus WD-40 motif (SEQ ID NO:262), were identified and examined for WD-40 repeats. Ten additional proteins containing WD-40 repeats were identified with this 35 strategy. The amino acid sequences of those proteins, with the WD-40 repeats aligned and delineated, are shown in Figs. 11, 19, 28, 31-33, 36, 39, 41 and 51. The sequences are represented in

the Sequence Listing as SEQ ID NO:28, 36, 45, 48-50, 53, 56, 58, and 68.

Other types of searches may be equally effective at identifying proteins which may contain WD-40 repeats. For example, on-line databases such as GenBank or SwissProt can be searched, either with an entire sequence of a WD-40-containing protein, or with a consensus WD-40 repeat sequence. Various search algorithms and/or programs may be used, including FASTA, BLAST or ENTREZ. FASTA and BLAST are available as a part of the GCG sequence analysis package (University of Wisconsin, Madison, Wisconsin). ENTREZ is available through the National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD.

Sequences identified with a protein homology search are then analyzed as described in parts A, B and C, above, to identify potential WD-40 motifs. Once located, the motifs can be aligned, and effective binding peptides may be designed.

F. Identification of WD-40 regions in novel polypeptides.
WD-40 repeats may be identified in a novel polypeptide
by, for example, the methods described in parts A-D above. It
will be appreciated, however, that step A above (homology
matrix) is not required in the identification of WD-40 repeats.
Following the guidance of the present invention, one skilled in
the art may, for instance, identify a WD-40 motif while scanning
the sequence of some, perhaps novel, polypeptide merely through
a recognition of one or more of the features characteristic of
WD-40 repeats.

The precise methods by which one skilled in the art arrives at the conclusion that a particular motif is a WD-40 repeat is less relevant to the present invention than is the use of sequences derived from WD-40 motifs, regardless of how they are identified, to design peptides effective to alter or modulate the activity of one member of a pair of interacting proteins and/or to disrupt protein-protein interactions.

35 VI. Identification of Activity-altering Peptides.

Upon the alignment and recognition of WD-40 repeats in a particular protein, one may proceed to design a peptide or a set of peptides that may be effective to associate with or bind to the protein with which the WD-40-containing protein normally associates. Such a binding or association may be expected to alter or modulate the activity of the protein and/or disrupt the association of the pair of interacting proteins.

The sequence of such a peptide will typically be homologous, if not identical to, a contiguous amino acid 10 sequence contained within at least one of the WD-40 repeats. Examples of the selection of WD-40-derived peptides effective to disrupt protein-protein interactions are detailed in parts C and D below, for RACK-PKC and $G\beta/\gamma-\beta$ ARK interactions, respectively.

Choosing an appropriate region within a WD-40 repeat.

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Putative binding peptides may be selected from any portion of a WD-40 repeat. If it is desired to obtain a degree of discrimination between the various WD-40-containing proteins, peptides should be chosen from the region between, and not including, the amino-terminal and carboxyl-terminal conserved 20 sets. This "central region" typically shows greater sequence diversity between different WD-40-containing proteins than the terminal regions, and is roughly outlined by boxes in Figures 11-51, which show the amino acid sequences and aligned WD-40 repeats of various WD-40 repeat-containing proteins. Within the 25 central region, peptides should be selected from sequences that have little or no homology to any other known sequences, save the sequence(s) of the protein(s) targeted for disruption.

For example, peptides rIII (SEQ ID NO:4, seven amino acids) and rVI (SEQ ID NO:7, eight amino acids), are identical 30 to segments of RACK1 WD-40 repeats (III and VI, respectively) beginning five amino acids in from the amino termini of the WD-40 repeats from which they are derived (see Fig 1C, underlined segments). The WD-40 repeat segments corresponding to the binding peptides comprise the left portion of the central region 35 of the respective WD-40 repeats, and are not well-conserved in RACK1.

If it is desired to inhibit the interactions of, for example, all of the isoforms of a particular WD-40-containing protein family, a sequences is selected that includes a significant number of residues that are shared or highly 5 homologous among at least one WD-40 repeat of each of the targeted isoforms.

If, on the other hand, an isoform-specific reagent is desired, a sequence is selected from a WD-40 repeat(s) of a specific isoform, where that sequence does not include a significant number of residues that are identical or highly homologous to residues in WD-40 sequences from related isoforms.

B. Choosing an appropriate length for a peptide.

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Effective binding peptides may be designed that range in length from as few as about four residues to 40 or more residues. Preferably, binding peptides will have a length of at least about six residues, and less than about 20 residues. length will be determined in part by the degree of desired homology to other WD-40 repeats, as described in part A above, and by the level of discrimination between proteins that is 20 required.

For example, binding peptides selected from RACK1 sequences to inhibit RACK1/PKC interactions were seven and eight amino acids in length. The peptides are long enough to bind specifically to the targeted sequences, but short enough to not cross-react with other WD-40 repeat binding proteins. These properties enable the peptides to have very selective and specific effects, as is shown below in Examples 6-11.

C. Design of RACK1 WD-40-derived peptides to inhibit RACK1-PKC interactions.

Peptides rIII (SEQ ID NO:4, seven amino acids) and rVI (SEQ ID NO:7, eight amino acids) were designed in part following the guidance presented in parts A and B above. The peptides are identical to segments of RACK1 WD-40 repeat sequences beginning five amino acids in from the amino termini of the WD-40 repeats from which they are derived. The WD-40 repeat segments corresponding to the binding peptides comprise the left portion

PCT/US95/01210

WO 95/21252

- 30 -

of the central region of the WD-40 repeats. The peptides were tested for their ability to disrupt protein-protein interactions in vitro and in vivo, as described in section VII and Examples 6-11 below.

Peptides derived from WD-40 repeats of Human G-Beta D. inhibit interactions of G-Beta subunits with β ARK.

Methods described in section V part E were used to identify WD-40 repeats (SEQ ID NO:128-134) in Human G-Beta (SEQ ID NO:41). Segments from the first six WD-40 repeats were 10 selected for the design of G-beta binding peptides (SEQ ID NO:13-18). The segments were selected based on criteria detailed in parts A and B, above.

The G-beta binding peptides are used to disrupt the interactions of G-beta subunits with β ARK. The disruption is 15 assayed using a modification of the overlay assay described in Example 4.

VII. Testing of Putative Binding Peptides.

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Detailed below are several assays by which the efficacy of WD-40-derived peptides at binding to a target 20 protein, inhibiting protein-protein interactions, and altering or modulating the activity of a target protein may be determined.

One class of assays, widely-used to assess the binding of two proteins to each other, are overlay assays. Overlay 25 assays are generally applicable to most proteins. They can be used to, for example, assess the binding of WD-40-derived peptides to their targets, as shown in Example 6 and described in part B below. Overlay assays can also be used to assess the ability of WD-40-derived peptides to inhibit the binding of two 30 interacting proteins, one of which contains a WD-40 motif from which the peptides were derived (see, for instance, Example 4 and part C below).

Other assays may be used to assess effects of WD-40derived peptides on the activity of the target protein. 35 assays may be in vivo assays, in vitro assays, or a combination of in vivo and in vitro assays. The assay used will depend on

- 31 -

the proteins involved and on the system(s) and/or process(es) that involve the interacting proteins against which the peptide was targeted. For instance, the assays described in parts D-I below are appropriate for characterizing PKC activity in vivo and in vitro.

While many of the assays below are particularly useful for characterizing the activity of PKC, they also illustrate a general framework of experiments by which the effects of WD-40 derived peptides on other proteins may be assessed.

10 A. Overlay assays to evaluate efficacy of putative binding peptides derived from WD-40 regions.

An overlay assay can be used to assess the disruption of the ability of a pair of proteins to associate. Methods for conducting overlay assays are well-known in the art (see, for example, Mochly-Rosen, et al., 1991).

Applications of overlay assays to evaluate putative binding peptides for PKC/RACK1 interactions are presented in Examples 4 and 5 herein. The assays can be generally described as follows.

One protein of a pair of interacting proteins
("immobilized" protein) can be resolved on an SDS/PAGE gel and
blotted onto an appropriate membrane (for example,
nitrocellulose or nylon) by methods known to those skilled in
the art. The blots may then be contacted with a solution

25 containing the other protein of the pair of interacting proteins
("overlay" protein) in the presence, and in the absence of
putative binding peptides. Following appropriate wash steps,
bound overlay protein can be detected by the use of an
appropriate probe, such as an antibody directed against the
overlay protein.

A variation on the above protocol may be performed to minimize a possible interference between unbound binding peptide and antibodies used to detect the presence of bound overlay protein. The modification consists of performing another

35 SDS/PAGE electrophoresis between the steps of binding the overlay protein, and detecting the overlay protein with antibody or other probe. It is accomplished by cutting the blot into

PCT/US95/01210 WO 95/21252

- 32 -

pieces sized to just encompass the area occupied by the blotted immobilized protein, after the overlay protein had been contacted (in the presence or in the absence of binding peptides) and allowed to bind to the blot. The pieces of 5 membrane are then incubated in a sample buffer, placed in the wells of a second SDS polyacrylamide gel and subjected to electrophoresis.

Following electrophoresis, the gel is blotted as above, and contacted with a probe, for example antibodies, to 10 detect bound overlay protein.

Binding of β PKC to peptides homologous to a WD-40 В. region of RACK1.

The binding of β PKC to peptide I (SEQ ID NO:1), peptide rVI (SEQ ID NO:7) and control peptide (SEQ ID NO:9) was 15 assessed in Example 6 using a PKC overlay assay similar to that described in Example 3. Increasing amounts of peptides were applied onto nitrocellulose using a slot-blot apparatus. The membranes were incubated with PKC in the presence and absence of PS, DG, and calcium.

The data are shown in Figure 4, and show that activated PKC bound to both peptides I and rVI at peptide amounts as low as 5 μ moles, but not to the control peptide. Unactivated PKC did not bind to peptide I, but did bind to peptide rVI at similar concentrations.

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The results indicate that while the peptides were homologous to one another and were capable of binding to the same protein, they behaved differently. Peptide rVI (SEQ ID NO:7; 8 residues) was able to bind to both activated as well as unactivated forms of PKC, whereas peptide I (SEQ ID NO:1; 15 30 residues) could bind only to activated PKC. The differences between the binding properties may be due, for example, to charge differences and/or length differences between the two peptides.

- 33 -

C. Effects of peptides homologous to WD-40 region of RACK1 on PKC binding to RACK1

Two peptides (peptide rIII; SEQ ID NO:4 and peptide rVI; SEQ ID NO:7) identical to regions of RACK1 WD-40 repeats (underlined, Figure 1C) were tested for their ability to inhibit PKC binding to recombinant RACK1 using a modification of the overlay procedure referred to above. The experiment is detailed in Example 4 and the results are shown in Figure 3.

Peptide I caused an 81±6% inhibition of PKC binding to recombinant RACK1 as compared with binding in the absence of added peptide. Both peptides rIII and rVI inhibited the binding of PKC to RACK1. In addition, peptides rI and rII were also effective inhibitors of the interaction of PKC to RACK1. A lesser inhibitory effect was obtained with peptides rIV and rV and no inhibition was obtained with peptide rVII.

The difference in the peptide's ability to inhibit binding may reflect differences in the roles played by the corresponding WD-40 repeats in the protein-protein interactions between PKC and RACK1. The peptide's ability or inability to inhibit protein-protein interactions as assayed by an overlay assay, however, is not necessarily correlated with the effects those peptides may have on the activity of the targeted proteins, as measured by both in vivo and in vitro assays and described in parts D-I below.

D. <u>Effects of peptides homologous to WD-40 regions of</u> RACK1 on PKC-mediated oocyte maturation.

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Peptides I (SEQ ID NO:1), rIII (SEQ ID NO:4) and rVI (SEQ ID NO:7) were also tested for their ability to affect insulin-induced, PKC-mediated maturation in *Xenopus* oocytes, as detailed in Example 7 and shown in Figures 5A and 5C.

PKC is involved in the maturation of Xenopus oocytes. Phorbol esters, which activate PKC, or microinjection of a constitutively active mutant of PKC induce the first stage of oocyte maturation in the absence of hormones. Exposure to insulin causes an increase in diacylglycerol levels and microinjection of activated PKC enhances insulin-induced maturation (Stith, et al.). Microinjection of purified RACK

proteins causes a significant decrease in the rate of oocyte maturation (Smith, et al., 1992). The insulin-induced oocyte maturation assay therefore provides an effective in vivo assay for compounds that interfere with the function of PKC.

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(Fig. 5B).

The maturation response was quantified by monitoring the appearance of a white spot in the animal hemisphere of the oocyte, indicating germinal vesicle breakdown (GVBD) and maturation. The indicated peptides were microinjected into Xenopus oocytes and the percent of oocytes with GVBD following 10 insulin exposure was plotted as a function of time in Figures 5A and C.

Approximately 80-85% of sham-injected (control) oocytes exposed to insulin reach maturation, as compared with 45-50% of oocytes injected with peptide I. The rate of 15 maturation of those oocytes that did mature was similar in the two cases. In contrast the effects of peptide I, both peptides rIII and rVI potentiated the effects of insulin on oocyte maturation, both in terms of the rate of maturation, and in the total fraction of oocytes that mature during the experiment. 20 Injection of peptides rIII or rVI increases the fraction of maturing oocytes to essentially 100%. Furthermore, peptide rVI induced oocyte maturation in the absence of insulin stimulation

Together, the data above indicate that peptides 25 homologous to the WD-40 region of RACK1 can modulate the function of a protein with which RACK1 interacts (e.g. PKC), that the modulation can occur in vivo, and that it can have clear and profound physiological consequences. Furthermore, the results with peptide rVI suggest that under appropriate 30 circumstances, the peptide alone may act to activate PKC, in the absence of other activating substances.

E. Effects of peptides homologous to WD-40 regions of RACK1 on PKC translocation in Xenopus oocytes.

Insulin causes the redistribution of β PKC, but not 35 other PKC isozymes, from a cytosolic form to a membraneassociated form, as evidenced by the relative levels of PKC in the soluble vs. the particulate fraction of oocyte homogenate.

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To assess the effects of RACK1 WD-40-derived peptides on insulin-induced PKC translocation, 50 nl of a 20 mM NaCl solution containing the indicated peptides were microinjected into Xenopus oocytes. The oocytes were then homogenized, and 5 the relative amount of PKC in the soluble and particulate fractions was assayed. The protocol followed was a modification of a method described by Smith, et al (1992). The results are shown in Figure 6.

Peptide I (50 μ M) did not affect β PKC distribution in 10 untreated oocytes, but inhibited insulin-induced β PKC translocation (Fig. 3, lanes 7,8). In contrast, peptide rVI (50 μ M) induced β PKC translocation in the absence of insulin treatment (Fig. 3, lanes 3,4). These results suggest that peptide I is an antagonist of hormone-induced PKC translocation, 15 whereas peptide rVI is an agonist and an activator of PKC translocation. In light of the results presented in Example 7, the data also suggest that the inhibition of insulin-induced GVBD following microinjection of peptide I was due to an inhibition of β PKC translocation.

Effects of peptides homologous to WD-40 regions of F. 20 RACK1 on sensitivity of β PKC to Arg-C endopeptidase.

Upon activation of PKC, a pseudosubstrate autoinhibitory sequence at the N-terminus of PKC dissociates from the catalytic site and renders the molecule sensitive to 25 endopeptidase Arg-C (Orr, et al.). Exposure of activated β PKC to Arg-C results in a limited proteolysis, or "nicking" of the enzyme. The nicking typically generates a 78 kDa fragment and several small fragments. Continued exposure to Arg-C typically results in the disappearance of β PKC (Orr, et al.).

Since peptides rIII (SEQ ID NO:4) and 'rVI (SEQ ID NO:7) exhibited PKC agonist activities in other assays (see, for instance Examples 7 and 8), experiments were performed to determine whether the peptides were capable of activating PKC in a manner to make it susceptible to endopeptidase Arg-C. The 35 experiments are detailed in Example 9 and the results are shown in Figure 7.

15

In the presence of effective concentrations of PKC activators (0.8 $\mu g/ml$ DG, 50 $\mu g/ml$ PS and 1 mM CaCl₂), exposure of β PKC to Arg-C resulted in nicking, generating the 78 kDa fragment (Fig. 7, lane 2). In the absence of PKC activators, 5 exposure of β PKC (80 kDa) to endopeptidase Arg-C had no effect on the enzyme (Fig 7, lane 1).

Incubation of β PKC with Arg-C at low concentrations of activators (2.5 $\mu \text{g/ml}$ PS and 50 μM CaCl₂) in the absence of added peptide, in the presence of control peptide (SEQ ID NO:9) and in 10 the presence of peptide I (SEQ ID NO:1) did not result in appreciable nicking activity (Fig. 7, lanes 4, 8 and 9, respectively). However, incubation of β PKC with the same low concentration of activators in the presence of peptides rIII or rVI resulted in the appearance of the 78 kDa nicked PKC fragment (effects of peptide rVI in Fig. 4, lanes 5-7). Concentrations as low as 10 nM of peptide rVI were sufficient to result in nicking activity, indicative of β PKC activation.

The results indicate that peptides rIII and rVI, but not peptide I, are effective to stabilize PKC in an activated conformation that renders it susceptible to Arg-C under conditions of low PKC activators that would otherwise not render the enzyme susceptible to Arg-C.

Effects of peptides homologous to WD-40 regions of G. RACK1 on β PKC autophosphorylation.

25 Activated PKC is capable of autophosphorylation, which can be assayed by incubation with $[\gamma^{-32}P]$ ATP and visualized on an autoradiograph of a gel. Anti-pseudosubstrate antibodies were shown previously to induce autophosphorylation in the absence of PKC activators (Makowske, et al.). Since peptide rVI (SEQ ID 30 NO:7) was effective to induce PKC translocation and GVBD in the absence of PKC activators, experiments were performed to determine if the peptide was also capable of inducing PKC autophosphorylation. The experiments are detailed in Example 10 and the data are shown in Figure 8.

PKC activated with PS (50 μ g/ml), DG (0.8 μ g/ml) and 35 $CaCl_2$ (1 mM) shows normal levels of autophosphorylation (lane 1). No autophosphorylation was seen in the absence of PKC activators

PCT/US95/01210 WO 95/21252

- 37 -

(lane 2), or in the absence of PKC activators with peptide I (SEQ ID NO:1; lane 5) or control peptide (SEQ ID NO:9; lane 6). In contrast, peptide rVI in the absence of PKC activators induced PKC autophosphorylation to over 80% of the levels 5 obtained for PKC alone in the presence of optimal concentration of PS, DG, and calcium (compare Fig. 8 lane 1 (control) with lane 4 (peptide rVI)).

Effects of peptides homologous to WD-40 regions of Η. RACK1 on histone phosphorylation by β PKC.

Another measure of PKC activity is the ability of activated PKC enzyme to phosphorylate histones. PKC phosphorylation of histone was carried out using a modification of the protocol described by Mochly-Rosen, et al., (1987). Phosphorylation was carried out in the presence or absence of 15 PKC activators (PS, DG and calcium) and RACK1-derived peptides. Phosphorylated histone was detected by autoradiography, following SDS-PAGE on a 10% gel.

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Since peptide rVI (SEQ ID NO:7) was effective to induce the autophosphorylation of PKC in the absence of PKC 20 activators, and both peptides rIII (SEQ ID NO:4) and rVI rendered PKC susceptible to proteolysis by Arg-C, experiments were performed to characterize the effect of the peptides on histone type III phosphorylation by PKC. The experiments are detailed in Example 11 and the results are shown in Figures 9 25 and 10.

The results are similar to those obtained for the effects of peptide rVI on autophosphorylation of PKC, that is, peptide rVI was effective to induce PKC-mediated histone phosphorylation in the absence of the PKC activators PS, DG, and 30 calcium, once again supporting that peptide rVI is an agonist of PKC activation. Peptide rIII similarly induced histone phosphorylation (Fig. 10).

PCT/US95/01210 WO 95/21252

- 38 -

VIII. Utility.

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Peptides as probes for the identification of target proteins.

WD-40 derived peptides may be used, for example, to 5 isolate clones encoding target proteins from an expression library. Variations on the cloning methods described herein can be used to identify clones expressing sequences capable of binding the peptides. For example, WD-40 derived peptides may be used to detect a target protein on a membrane using a 10 standard binding assay. Positive clones may be detected, for example, by radiolabeling the peptides and exposing the membrane to film.

Target proteins isolated in this manner may be completely novel, or they may be partially characterized (in 15 terms of a biological activity in a homogenate, or a band on a protein gel, for example).

Upon isolation of a cDNA encoding a binding protein, the cDNA may be expressed, for example, as detailed herein, and the protein may be characterized. Purified protein thus 20 isolated may be used for a number of applications, including the production of antibodies.

Peptides designed according a method of the present invention may also be used, for example, as probes in a Western blot of a tissue homogenate to identify and determine the 25 molecular weight of known or putative target proteins.

Screens such as those described above may be facilitated by the modification of peptides used for screening to incorporate any of a variety of reporter moieties. example, the peptides can be radiolabeled with 125I.

30 Alternatively, the peptides can be modified with a sequence-tag or a ligand for an affinity column by methods known to those skilled in the art.

The peptides may also be modified to covalently crosslink to their targets after binding, for example with any of various affinity reagent for cross linking known to those skilled in the art. This enables the isolation of target proteins that bind the peptides relatively weakly.

- 39 -

B. <u>Peptides as substitutes for defective WD-40 containing proteins.</u>

In cases where a WD-40 containing protein is implicated in a disease (see, for example Reiner, et al.),

5 peptides derived from WD-40 regions of the defective protein may be used as substitutes, for example, to activate a target enzyme. Such an approach may be more feasible than attempting therapy with intact proteins. The approach has an additional advantage in that it does not require knowledge of the

10 chromosomal location of the affected gene.

The peptides can be introduced into affected cells by any of several methods known to those skilled in the art, including through the use of an appropriate expression vector or through *in vitro* synthesis and administration by an effective, expedient route. In vitro studies can be carried out using skinning or microinjection techniques.

C. Peptides as pharmaceutical agents.

25

WD-40 derived peptides of the present invention may be used therapeutically, as described above. Such peptides may be designed so as to interact with endogenous target molecules to augment or correct their function. Alternatively, peptides may be designed to specifically interact with target molecules unique to a pathogenic organism.

D. <u>Peptides as modulators of enzyme activity of proteins</u> involved in protein-protein interactions.

Peptides synthesized according to a method of the invention may be effective to modulate the function of a target molecule (e.g. serve as agonists or antagonists). As shown herein, for example, peptides rVIII and rVI can serve to activate or enhance the activation of PKC, whereas peptide I can inhibit PKC.

These activities may be used in screens to identify other compounds which may affect the function of target molecules such as PKC. In particular, because WD-40 derived peptides may interact with PKC in a manner that is more similar to in vivo interactions (i.e. protein binding), they may be

- 40 -

useful for identifying molecules or compounds that may interfere with PKC function in vivo, but might not necessarily interfere with PKC in vitro.

For example, peptide rVI can be used to stimulate PKC in the absence of traditional PKC activators, and the rVI-stimulated enzyme may be used in a screen to identify, for example, novel PKC-inhibiting or PKC-potentiating compounds.

If constitutive activation or inactivation of a target enzyme is desired, peptides may be designed with integrated or derivatized cross-linking moieties. The peptides can be cross-linked to their targets upon binding such that the target molecule assumes the desired state of activity for the lifetime of the target molecule.

Conversely, as described herein for PKC, peptides may also be designed so as to accelerate the degradation of the target molecule. For example, peptide rIII accelerated the degradation of PKC in cardiac myocytes.

E. WD-40 derived peptides as specific modulators of isozymes.

Peptides designed according to a method of the present invention can also be used to provide target isozyme-specific modulator molecules. For example, most cells have several PKC isozymes, all of which are activated by the same cellular stimuli. Determining the function of the individual isozymes is therefore difficult.

WD-40 derived peptides that selectively stimulate or inhibit specific target isozymes or groups of isozymes may be useful, both in terms of therapeutic value, and in terms of determining the roles of different isozymes in cellular function and disease. Such information can be useful for the identification of new molecular targets for drug development, as is described in part F, below.

- 41 -

F. Compounds designed based on the predicted structure of binding peptides as pharmaceutical agents.

Peptides derived from WD-40 repeats may be useful for identifying lead compounds for drug development. Peptides as small as 7 residues have been shown herein to possess specific bioactivities upon interaction with their targets in vivo. The structure of such small peptides can be readily determined by a number of methods, such as NMR and X-ray crystallography. A comparison of the structures of peptides similar in sequence, but differing in the biological activities they elicit in the target molecules, can provide information about the structure-activity relationship (SAR) of the target enzyme.

For example, peptide I and RACK1-derived peptides rIII (SEQ ID NO:4) and rVI (SEQ ID NO:7) had opposite effect in vivo, although they are homologous in sequence.

Information gleaned from the examination of structureactivity relationships can be used to design either modified
peptides, or other small molecules or lead compounds which can
be tested for predicted properties (e.g. agonist or antagonist),
20 as related to the target enzyme. The activity of the lead
compounds can be evaluated using assays similar to those used in
the evaluation of peptide-binding effects.

Information relating to a SAR of a target enzyme may also be obtained from co-crystallization studies. In such studies, a peptide with a desired activity is crystallized in association with a target protein, and the X-ray structure of the complex is determined. The structure can then be compared, for example, to the structure of the target protein in its native state, and information from such a comparison may be used to design compounds expected to possess specific activities. The compounds can be evaluated using assays similar to those used in the evaluation of peptide-binding effects.

G. PCR of cDNA corresponding to WD-40 repeats to identify mutations in WD-40 containing proteins.

Results presented herein suggest that the middle regions of WD-40 motifs are involved in the association of a WD-40 protein with its target protein. Because this association

WO 95/21252

- 42 -

is likely to play a central role in the activity of a polypeptide complex comprised of interacting proteins, some genetic diseases may include mutations at these regions of WD-40 Therefore, if a WD-40 containing containing proteins. 5 protein is implicated in a genetic disorder, it may be possible to use PCR to amplify DNA from the WD-40 regions to quickly check if a mutation is contained within one of the WD-40 motifs. Primers can be made corresponding to either (i) the flanking regions of each repeat or (ii) the flanking regions of a series 10 of tandem repeats from the affected gene. Standard sequencing techniques can be used to determine whether a mutation is present. This method does not require prior chromosome mapping of the affected gene and can save time by obviating the need to sequence the entire gene encoding a defective WD-40 protein.

WD-40 based polypeptides as affinity ligands

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Since the polypeptide compositions of the invention are able to bind proteins of interest, generically called a "first protein", the polypeptide compositions can also be used to retrieve the proteins of interest from samples and the 20 peptides can be used as affinity ligands for chromatographic procedures to purify and analyze said proteins. Standard chromatographic techniques are employed. Typically, the polypeptide is coupled to a solid support and the sample putatively containing the first protein is contacted with the 25 polypeptide composition of the invention; any unbound components of the sample are removed and, if desired, the first protein, bound to support, is eluted and recovered.

> Use of peptides in screening tests for candidates I. Various candidate compounds, not necessarily

30 polypeptides, may be shown to bind to a first protein using the polypeptides of the invention as competitors. screening assays, the ability of a candidate compound to bind a first protein can be assessed by contacting the first protein with the polypeptide composition of the invention in the 35 presence and absence of the candidate compound and evaluating the level of binding of the polypeptide in the presence as opposed to the absence of the candidate. Decreased binding of

PCT/US95/01210 WO 95/21252

- 43 -

the polypeptide in the presence of the candidate indicates that the candidate binds to the first protein.

More broadly, the interaction of a protein with a polypeptide subsequence contained in the second protein can be 5 assessed by contacting the first protein with a polypeptide representing the subsequence and observing any interaction with the polypeptide composition.

Production of the Peptides of the Invention IX.

The polypeptides of the invention can be prepared 10 using standard techniques for the synthesis of peptides from amino acids. Such techniques, when conducted in solid phase chemistry are available commercially.

The polypeptides of the invention may also be produced using recombinant methods. These methods are by now well known 15 in the art; DNA molecules containing nucleotide sequences encoding the desired polypeptides can readily be synthesized and ligated into expression systems for production of the peptides as is understood in the art. A wide variety of hosts is available, including procaryotic and eucuryatic hosts. The 20 construction of expression vectors, means to modify these hosts, and culturing the modified hosts for recombinant production of polypeptides are conducted using standard techniques.

The following examples illustrate, but do not limit the present invention.

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Materials and Methods

Nitrocellulose filters were obtained from Schleicher and Schuell (Keene, NH).

Synthetic peptides were prepared using commercially available automated peptide synthesizers. Alternatively, custom designed peptides may be purchased, for example, from Bachem Bioscience (King of Prussia, PA). Peptides may also be prepared recombinantly by expressing oligonucleotide sequences encoding the peptides. The oligonucleotide sequences may be either synthesized directly by standard methods of oligonucleotide synthesis, or, in 35 the case of large coding sequences, synthesized by a series of cloning steps involving a tandem array of multiple oligonucleotide fragments corresponding to the coding sequence (Crea; Yoshio, et al.; Eaton, et al.). Oligonucleotide coding sequences can be expressed by standard recombinant procedures (Maniatis, et al.; Ausubel, et al.).

"Triton" refers to a nonionic detergent comprising a polyoxyethylene ether and other surface-active compounds. An exemplary Triton detergent is "TRITON X-100", available from Sigma Chemical Company, St. Louis, MO.

"Tween" refers to a nonionic detergent comprising polyoxyethylenesorbitan monolaurate with a fatty acid composition of approximately 55% lauric acid, with a balance composed primarily of myristic, palmitic and stearic acids. An exemplary Tween detergent is "TWEEN 20", available from Sigma Chemical Company, St. Louis, MO.

"SDS" refers to sodium dodecyl sulfate.

"PAGE" refers to polyacrylamide gel electrophoresis.

"IPTG" refers to isopropyl ß-D-thiogalactopyranoside.

Example 1

Expression Cloning of a PKC-binding Protein

20 A. Buffers.

30

Overlay block buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 3% bovine serum albumin (BSA) and 0.1% polyethylene glycol.

Overlay buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1 % BSA, 1% polyethylene glycol, $10\mu g$ per ml soybean trypsin inhibitor and $10\mu g$ per ml leupeptin.

B. <u>Isolation of a PKC-binding cDNA clone by an overlay</u> assay.

A rat brain (Sprague Dawley) cDNA expression library, constructed in the lambda phage cloning vector "UNI-ZAP XR" (Stratagene, La Jolla, CA), was screened by an overlay assay as follows.

Lifts of nitrocellulose filters from IPTG-induced cDNA library plates were incubated for 2 hours in overlay block buffer. The filters were then transferred to overlay buffer with or without 1 unit of a mixture of rat brain PKC isozymes $(\alpha, \beta, \gamma, \delta, \epsilon)$ and $(\alpha, \beta, \gamma, \delta, \epsilon)$ are $(\alpha, \beta, \gamma, \delta, \epsilon)$ and $(\alpha, \beta, \gamma, \epsilon)$ and $(\alpha, \beta, \epsilon, \epsilon)$ and $(\alpha, \delta, \epsilon, \epsilon$

at room temperature with PKC activators (60 μ g/ml phosphatidylserine (PS), 2 μ g/ml diacylglycerol (DG), 1 mM CaCl₂).

Following three 15 minute washes in the overlay buffer, the filters were incubated in the overlay block buffer in the presence of a mixture of monoclonal anti- α , β and γ PKC antibodies (1:1000 dilution; Seikagaku Kogyo, Tokyo, Japan) and polyclonal anti- δ , ϵ and ζ PKC antibodies (1:500 dilution; Life Technologies, Gaithersburg, MD). After a 16 hr incubation at room temperature, the filters were washed three times, 15 minutes per wash, in overlay buffer.

Binding of PKC was determined using alkaline phosphataseconjugated goat anti-rabbit or goat anti-mouse antibodies (1:2000 dilution, Boehringer Mannheim Biochemicals, Indianapolis, IN). The alkaline phosphatase reaction used 5-bromo-4-chloro-3-indoyl phosphate p-toluidine salt as a substrate, and was performed following the manufacturer's protocol.

Library screening of 2.4 x 10⁶ recombinant "UNI-ZAP" lambda phage plaques yielded one clone, pRACK1, that reacted with arti-PKC antibodies in the PKC overlay membrane, but not in the control overlay membrane. These results suggest that pRACK1 encodes a PKC binding protein.

C. Cloning and sequencing cDNA from positive plagues.

The clone pRACK1, identified as detailed in part B above, was plaque purified and cDNA inserts were isolated as phagemids by in vivo excision of the cloning vector, according to the manufacture's protocol (Stratagene, La Jolla, CA). DNA sequencing of pRACK1 was carried out using standard di-deoxy sequencing techniques (Maniatis, et al.) The DNA sequence of RACK1 is shown in Figure 1A. The sequence is also contained in the Sequence 30 Listing as SEQ ID NO:19.

Example 2

Expression and Purification of Recombinant RACK1 Protein in E. coli

A PstI/XhoI DNA fragment containing an open reading frame 35 of 317 amino acids from the putative translation start site of pRACK1 (see underlined ATG in Fig. 1A) and 8 additional nucleotides - 46 -

upstream of the initiating methionine was subcloned into E. coli expression vector pMAL-c2 (New England BioLabs, Beverly, MA). This vector contains the malE gene, which encodes maltose-binding protein (MBP). Induction of E. coli containing the vector results 5 in the production of an MBP-fusion protein (Ausubel, et al.). The vector also includes a recognition site for the protease factor Xa, which allows the protein of interest to be cleaved from MBP after purification without adding any vector-derived residues to the protein.

A culture of TB1 E. coli transformed with RACK1containing pMAL-c2 was induced by a 3 hr incubation with 1.8 mM A protein fraction containing a 78 kDa fusion protein, comprised of RACK1 fused to MBP was isolated from the cultured E. coli by standard methods (Ausubel). The fusion protein was amylose affinity column according to purified on an 15 manufacture's protocol (New England BioLabs, Beverly, MA) and incubated with protease Xa (New England BioLabs) to yield a 36 kDa protein (RACK1) and a 34 kDa protein (possibly a RACK1 degradation product).

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Example 3

Binding of PKC to Recombinant RACK1

Buffers. Α.

PBS/Tween buffer: 140 mM NaCl, 8 mM Na₂PO₄, 1.5 mM KH₂PO₄, 3 mM KCl and 0.05% Tween at pH 7.0.

Overlay wash buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1% polyethylene glycol and 0.1 mM CaCl₂.

В. Overlay assay.

Purified recombinant RACK1 protein (100-250 µg per lane, produced as detailed in Example 2) was subjected to SDS/PAGE and (Ausubel). 30 blotted onto nitrocellulose membranes The nitrocellulose membranes were cut into strips, which were incubated for 0.5 hr in overlay buffer (Example 1) in the presence or absence of a mixture of PKC isozymes (α , β , γ , δ , ϵ and ζ , ~10 nM each concentration) μg/ml final and PKC activators (60 35 phosphatidylserine (PS), 2 $\mu g/ml$ diacylglycerol (DG), and 1 mM CaCl₂). Unbound material was removed by five washes, 5-min each,

- 47 -

in overlay wash buffer. Where indicated, PKC activators were present during the incubation of PKC with the nitrocellulose strips. The conditions for each sample and corresponding results are presented in part D below.

C. <u>Detection of bound PKC</u>.

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PKC bound to RACK1 immobilized on nitrocellulose strips was detected as follows. The strips were incubated for 16 hours at room temperature with a mixture of anti-PKC antibodies as detailed in part B of Example 1, and then washed three times, 15 10 minutes per wash, with PBS/Tween buffer. The strips were incubated with anti-mouse and anti-rabbit horseradish peroxidase-linked secondary antibodies (Amersham Life Science, Arlington Heights, IL) diluted 1:1000 in PBS/Tween buffer supplements with 2% BSA, for 1 hour at room temperature. After washing three times, 15 minutes 15 per wash with PBS/Tween buffer, the strips were subjected to a chemiluminescent reaction with luminol (diacylhydrazide) detailed in the maufacturer's protocol (Amersham Life Science, Arlington Heights, IL), followed by an immediate exposure to autoradiography film (Eastman Kodak, Rochester, NY) for 30 seconds 20 to 5 minutes.

D. <u>Effects of PKC activation on PKC binding to RACK1</u>.

The results presented in Figure 2 show the influence of PKC activators on the binding of PKC to RACK1 immobilized on nitrocellulose membranes. The overlay assay was carried out as described in part B above. The test reagents contained in each sample and the corresponding lanes on the blot presented in Fig. 2 are as follows. Lane 1: PKC, 60 µg/ml PS, 2 µg/ml DG and 1 mM CaCl₂; lane 2: PKC and 1 mM EGTA; lane 3: PKC, 60 µg/ml PS and 2 µg/ml DG; lane 4: PKC and 1 mM CaCl₂; lane 5: No PKC added; lanes 6 and 7: PKC, 60 µg/ml PS 2 µg/ml DG, 1 mM CaCl₂, and 10 µM substrate peptide (SEQ ID NO:11; lane 6) or 10 µM pseudosubstrate peptide (SEQ ID NO:12; lane 7). The results are representative of three independent experiments.

It can be appreciated that the binding of PKC as detected by anti-PKC antibodies is minimal in the presence of EGTA or calcium alone (Fig. 2, lanes 2, 4, respectively), is greater in the

- 48 -

presence of phosphatidylserine (PS) and diacylglycerol (DG; lane 3), and is maximal in the presence PS, DG and calcium (lane 1). Antibody binding was not observed in the absence of added PKC (lane 5). Furthermore, maltose binding protein alone, or an extract from non-transformed E. coli did not bind PKC.

The concentration dependence of PKC binding to RACK1 was characterized with β PKC, since this isozyme is a major component of the PKC mixture used for the overlay assay. The mean half maximal binding was ~0.375 nM, and maximal binding was ~4 nM (n=3; values reflect binding of β PKC isozyme in the presence of other PKC isozymes and was determined by scanning autoradiograms in the linear range of detection, as described in Mochly-Rosen, et al., (1991).

The results presented above indicate that in order for PKC to bind to RACK1 it must be activated. In vitro, activation may be accomplished, for example, by phosphatidylserine and diacylglycerol, or, more preferably, by phosphatidylserine, diacylglycerol and calcium.

Example 4

Inhibition of PKC Binding to RACK1 by RACK1-specific WD-40-homologous Peptides

Assays for the inhibition of PKC binding to RACK1 by putative binding peptides were carried out by combining a variation of the overlay protocol described in Example 3 part B above, with an overlay extraction assay described in part B below. The variation in the overlay protocol consisted of incubating the putative binding peptides with a mixture of PKC isozymes for 15 minutes at room temperature before the mixture was used to contact the nitrocellulose strips containing immobilized RACK1.

A. Buffers.

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Sample buffer: 0.3 M Tris HCl, 5% SDS, 50% glycerol, 0.01% bromophenol blue and 5% β -mercaptoethanol.

- 49 -

Overlay extraction protocol. В.

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Nitrocellulose strips containing immobilized RACK1, that had been contacted with a solution containing a mixture of PKC isozymes, were washed and the area corresponding to the 36 kDa 5 (RACK1-containing) band was cut out. The pieces (containing PKC/RACK1 complexes) were incubated with sample buffer for 10 minutes at 80°C. The sample buffer and the nitrocellulose pieces were then placed in wells in the PAGE gel and subjected to SDS-PAGE to elute the bound proteins. The gel was blotted onto 10 nitrocellulose and a Western blot analysis was carried out using the mixture of antibodies (specific for PKC α , β , γ , δ , ϵ and ζ isozymes) described in Example 1 part B. Bound antibodies were detected by 125I-protein A.

C. PKC overlay in the presence of binding peptides.

Peptides derived from or homologous to WD-40 repeats of RACK1 were tested for their ability to inhibit PKC binding to recombinant RACK1. Binding of PKC to RACK1 was carried out using a variation of the overlay procedure described in Example 3 part In the experimental samples, peptides were incubated with a solution containing a mixture of rat brain PKC isozymes (~10 nM each) for 15 minutes at room temperature.

Following completion of the modified overlay protocol, the samples were subjected to the overlay-extraction protocol detailed in part B, above.

The results in Figure 3 show the binding of PKC to RACK1, carried out without (lane 1) or with (lanes 2-4) a preincubation of peptides with PKC. Lane 2 shows PKC binding following a preincubation with 10 μM peptide I (SEQ ID NO:1). Peptide I caused an 81±6% inhibition of PKC binding to recombinant RACK1 as compared 30 with binding in the absence of added peptide (n=3). Lanes 3 and 4 show PKC binding following a preincubation with 10 μ M peptide rIII (SEQ ID NO:4) and 10 μ M peptide rVI (SEQ ID NO:7), respectively. Both peptides inhibit the binding of PKC to RACK1. It can be seen that peptide rIII is somewhat more effective than The results shown are representative of three 35 peptide rVI. independent experiments.

- 50 -

The overlay-extraction method (part B above) was used in experiments relating to the peptide inhibition of PKC binding in order to decrease the possibility that some part of the inhibition of PKC binding to RACK1 reflects an interference in the binding of anti-PKC antibodies to the PKC/RACK1 complexes. Free peptides are effectively removed from the PKC/RACK1 complexes during the second round of SDS/PAGE, prior to blotting and detection of immobilized PKC/RACK1 complexes by anti-PKC antibodies.

Example 5

10 Identification of Sequenced Proteins Containing WD-40 Repeats

A search for WD-40 motif-containing proteins was done using the ENTREZ program, release 6.0 (National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD). The ENTREZ database was searched for protein sequences related to the β subunit of transducin.

Protein sequences homologous to β -transducin were examined for the existence of WD-40 repeats, following the guidance for identification of WD-40 repeats presented in section V of the specification, above.

The proteins were also used to carry out additional searches of the database, in order to identify other proteins which may contain WD-40 repeats, but which might not be homologous to the β subunit of transducin. Sequences identified during the second round of searches were again examined for WD-40 repeats.

This search strategy identified 30 proteins containing WD-40 sequences. The amino acid sequences of these proteins, with the WD-40 regions aligned and delineated, are shown in Figs. 12-18, 20-27, 29-30, 34-35, 37-38, 40 and 42-50. The sequences are represented in the Sequence Listing as SEQ ID NO:29-35, 37-44, 46-47, 51-52, 54-55, 57 and 59-67. An examination of the sequences in the figures reveals that although there can be divergence between the WD-40 motifs of different proteins, a consistent pattern can be inferred based on the teachings presented in part V of the specification above.

An additional search, using a consensus WD-40 sequence (SEQ ID NO:262), was conducted with the "MACVECTOR" program

(Eastman Kodak Co., New Haven, CT) to search GenBank (December 1993 release). Default settings (matrix=250) were used for the search. The search identified the 250 proteins with the highest homology These proteins were examined, as to the consensus sequence. detailed in part V above, for WD-40 repeats. Ten additional proteins containing WD-40 repeats were identified with this strategy. The amino acid sequences of those proteins, with the WD-40 repeats aligned and delineated, are shown in Figs. 11, 19, 28, 31-33, 36, 39, 41 and 51. The sequences are represented in the Sequence Listing as SEQ ID NO:28, 36, 45, 48-50, 53, 56, 58 and 68.

Example 6

Binding of \(\beta \) PKC to RACK1 WD-40-derived Peptides

Buffers. Α.

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Peptide overlay block buffer: 20 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 3% bovine serum albumin (BSA) and 0.1% polyethylene glycol.

Overlay wash buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1% polyethylene glycol and 0.1 mM CaCl₂.

PKC overlay of immobilized peptides. В.

The binding of β PKC to peptide I (SEQ ID NO:1), peptide rVI (SEQ ID NO:7) and control peptide (SEQ ID NO:9) was assessed using a PKC overlay assay similar to that described in Example 3. Increasing amounts of peptides (0.5 μ mole, 1.0 μ mole, 5.0 μ mole and 10.0 μ mole) suspended in 20 mM NaCl were applied individually onto nitrocellulose using a slot-blot apparatus (Schleicher and Schuell, 25 Keene, NH). The nitrocellulose membrane was washed three times. 15 minutes per wash, in peptide overlay buffer and incubated for two hours in peptide overlay block buffer. The membrane was cut into sections and the sections were transferred to different PKC-30 containing solutions and incubated for 30 minutes at room temperature. All the solutions contained 5 nM rat brain PKC in peptide overlay buffer. Some solutions additionally contained PS, DG, and calcium. The membranes were then washed three times, 15 minutes per wash, in peptide overlay buffer and incubated in 35 peptide overlay block buffer containing anti- β PKC monoclonal antibodies (1:1000 dilution; Seikagaku Kogyo, Tokyo, Japan). After

- 52 -

a 16 hr incubation at room temperature, the filters were washed three times, 15 minutes per wash, in peptide overlay buffer.

Binding of PKC was determined using chemiluminescence as described in Example 3, part C. Quantitation of PKC binding was 5 carried out using a "MICRO SCAN" 1000 gel analyzer (Galai Inc., Yokneam, Israel).

The data show that activated PKC bound to both peptides I and rVI, but not to the control peptide, at peptide amounts as low as 5 μ moles. Unactivated PKC did not bind to peptide I, but 10 did bind to peptide rVI at similar concentrations.

The results indicate that peptide rVI is capable of binding both activated as well as unactivated forms of PKC, whereas peptide I binds only to activated PKC.

Example 7

Effects of RACK1 WD-40-derived Peptides on PKC-mediated Oocyte 15 Maturation

Exposure to insulin induces maturation in Xenopus oocytes via a PKC-dependent pathway (Smith, et al., 1992). The maturation response may be quantified by monitoring the appearance of a white 20 spot in the animal hemisphere of the oocyte, indicating germinal vesicle breakdown (GVBD) and maturation. To assess the effects of RACK1 WD-40-derived peptides on insulin-induced PKC-mediated maturation, 50 nl of a 20 mM NaCl solution containing the indicated peptides [peptide I (SEQ ID NO:1; ●), peptide rVI (SEQ ID NO:7; ■), 25 or injection solution (\square)] (peptides at 50 μ M) were microinjected into Xenopus oocytes. The symbols refer to symbols used in Figure 5, which shows the data from this example. One hour following the peptide injections, the oocytes were exposed to a solution containing insulin (8.25 μ g/ml) for 2 minutes (t=0). 10-15 oocytes were used for each sample.

The data, representative of three independent experiments, are expressed as the percent of oocytes with GVBD following insulin exposure and are plotted as a function of time in Figure 5.

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In oocytes injected with buffer or control peptide, onset of maturation was typically 4-5 hours after exposure to insulin. Following this delay, %GVBD followed an approximately exponential

- 53 -

time-course, reaching a plateau of about 85-90% GVBD at about 10-12 These data indicate that approximately 80-85% of shamhours. injected oocytes exposed to insulin at t=0 reach maturation, and that maturation is reached relatively quickly (within about 10 hours) relative to the time-course of the experiment (20 hours).

Oocytes injected with peptide I (SEQ ID NO:1) responded in a manner similar to control oocytes, except the plateau was at about 45-50% GVBD. These data suggest that injection of peptide I blocked maturation in approximately 40-45% of oocytes that would 10 normally proceed to maturation, but had little effect on the kinetics or extent of maturation of the remaining (50-55%) oocytes.

Oocytes injected with peptide rVI (SEQ ID NO:7) responded with a slightly shorter delay (about 3-4 hours), but reached a higher plateau (about 95-100% GVBD) more quickly (within about 5 15 hours) than control oocytes. These data suggest that peptide rVI potentiates the effects of insulin on oocyte maturation, both in terms of the rate of maturation, and in the total fraction of oocytes that mature during the experiment. Injection of peptide rVI increases the maturing fraction to essentially 100%

The effects of both peptides I and rVI on GVBD were dosedependent between 5 μ m-500 μ M.

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Since peptide rVI enhanced insulin-induced GVBD, experiments were performed to determine whether peptide rVI can induce GVBD in the absence of insulin. The data from these 25 experiments are shown in Fig. 5B. Microinjection of peptide rVI (50 μ M) alone, but not peptide I, control peptide or buffer, induced GVBD. Maturation initiated with a longer delay (about 6-7 hours) than in the control insulin-induced oocytes in Fig. 5A (about 4-5 hours), and reached a plateau of about 50% GVBD.

Together, the data above indicate that peptides homologous to the WD-40 region of RACK1 modulate the function of Peptide I inhibited PKC-mediated oocyte maturation by about 40%, whereas peptide rVI potentiated insulin-induced maturation, and resulted in a limited maturation response even in the absence The latter result suggests that peptide rVI, under 35 of insulin. appropriate circumstances, may act to activate PKC in the absence of other activating substances.

PCT/US95/01210 WO 95/21252

- 54 -

Example 8

Effects of RACK1 WD-40-derived Peptides on PKC Translocation in Xenopus Oocytes

A. Buffers.

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Homogenization buffer: 20 mM Tris HCl, pH 7.5, 10 mM EGTA, 2 mM EDTA, 0.25M sucrose, $10\mu M$ phenylmethylsulfonyl fluoride, $20\mu g/ml$ of each leupeptin and soybean trypsin inhibitor.

PKC translocation in oocytes. В.

Insulin causes the translocation of β PKC, but not other 10 PKC isozymes, from a cytosolic form to a membrane-associated form, as evidenced by the relative levels of PKC in the soluble vs. the particulate fraction of oocyte homogenate. To assess the effects peptides insulin-induced RACK1 WD-40-derived on translocation, 50 nl of a 20 mM NaCl solution containing the indicated peptides were microinjected into Xenopus oocytes. 15 oocytes were then homogenized, and the relative amount of PKC in the soluble and particulate fractions was assayed. The protocol followed was a modification of a method described by Smith, et al. The results are shown in Figure 6. (1992).

Batches of 50 oocytes were microinjected with either peptide rVI (SEQ ID NO:7; 50 μ M; lanes 3, 4), peptide I (SEQ ID NO:1; 50 μM , lanes 7, 8) or injection solution (NaCl 20 mM, lanes Homogenates from each batch were prepared 60 1,2 and 5,6). minutes after microinjection (lanes 1-4) or 60 minutes after 25 addition of insulin (lanes 5-8). The homogenates were centrifuged at 10,000 g for 3 minutes, the upper layer (containing fat and yolk) was removed, and the remainder was frozen at -70 °C. Prior to use, the samples were thawed, 200 μ l homogenization buffer was added and the samples were centrifuged at 100,000 g for 30 minutes The supernatants (soluble fraction) were removed and at 4 °C. "CENTRICON" concentrators concentrated to 20 μ l using The pellets (particulate fractions) were (Amicon, Beverly, MA). dissolved in 20 μ l of homogenization buffer. The samples were resolved on an 8% SDS/PAGE gel and blotted onto nitrocellulose. 35 The amount of PKC in each fraction was determined by Western blot using anti- β PKC antibodies (1:1000 dilution; Seikagaku Kogyo,

- 55 -

Tokyo, Japan). Bound primary antibodies were detected by chemiluminescence as described in Example 3, part C.

The antibodies showed immunoreactivity with an ~80 kDa protein that corresponds to βPKC . Data are representative of three experiments.

The data are shown in Figure 6. Lanes 1, 3, 5 and 7 contain particulate fractions (p), while lanes 2, 4, 6 and 8 contain soluble (cytosol) fractions (c). Peptide I (50 μ M) did not affect β PKC distribution in untreated oocytes, but inhibited insulin-induced β PKC translocation (Fig. 3, lanes 7,8). In contrast, peptide rVI (50 μ M) induced β PKC translocation in the absence of insulin treatment (Fig. 3, lanes 3,4).

The results above suggest that peptide I is an antagonist of insulin-induced PKC translocation, whereas peptide rVI is an agonist and an activator of PKC translocation. In light of the results presented in Example 7, the data also suggest that the inhibition of insulin-induced GVBD following microinjection of peptide I was due to an inhibition of β PKC translocation.

Example 9

20 Effects of RACK1 WD-40-derived Peptides on Sensitivity of PKC to Arg-C Endopeptidase

A. Buffers.

Sample buffer: 0.3 M Tris HCl, 5% SDS, 50% glycerol, 0.01% bromophenol blue and 5% β -mercaptoethanol.

25 B. <u>Nicking of βPKC by Arg-C endopeptidase</u>.

Upon activation of PKC, a pseudosubstrate autoinhibitory sequence at the N-terminus of the molecule dissociates from the catalytic site and becomes sensitive to endopeptidase Arg-C (Orr, et al.). In the absence of PKC activators, exposure of the 80 kDa β PKC to endopeptidase Arg-C has no effect on the enzyme (see Fig 7, lane 1). In the presence of the PKC activators PS, DG and calcium, however, exposure of β PKC to Arg-C results in a "nicking" of the PKC (i.e. limited proteolysis generating a 78 kDa fragment and several small fragments (see Fig. 7, lane 2)). Continued exposure to Arg-C results in the disappearance of β PKC (Orr, et al.). The present experiment tests whether peptides derived from

the WD-40 region of RACK1 alter the sensitivity of β PKC to endopeptidase Arg-C.

The methods used to assay Arg-C sensitivity are a modification of methods described by Orr, et al. Rat brain PKC (~ 5 5 nM) was incubated at room temperature in 500 μ l of 20 mM Tris-HCl buffer (pH 7.5) alone or with Arg-C (5 units/ml) in the presence or absence of the indicated peptides (final concentration 10 μM or as indicated), PS, DG, and calcium (as indicated). 50 μ l aliquots were removed into 20 μ l of sample buffer during the reaction as 10 indicated (samples in all the lanes were incubated for 30 minutes , except lanes 5, and 6, which were incubated for 5 and 15 minutes, respectively). The samples were boiled for 10 minutes at 80°C and β PKC was detected by Western blot loaded onto 8% SDS-PAGE. analysis using anti- β PKC antibodies as described in Examples 6 and 8.

The results are shown in Figure 7. PKC was incubated for the indicated time alone (lane 1) or in the presence of Arg-C (lanes 2-9), with DG (0.8 μ g/ml), PS (50 μ g/ml) and CaCl₂ (1 mM; lane 2), with PS (50 μ g/ml) and CaCl₂ (1 mM; lane 3), with PS (2.5 μ g/ml) and CaCl₂ (50 μ M; lane 4); with PS (2.5 μ g/ml), CaCl₂ (50 μ M) and with either peptide rVI (SEQ ID NO:7; 10 μM ; lanes 5-7), control peptide (SEQ ID NO:9; lane 8) or with peptide I (SEQ ID NO:1; lane 9).

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Incubation of β PKC with Arg-C at low concentrations of 25 activators (2.5 $\mu g/ml$ PS and 50 μM CaCl₂) in the absence of added peptide did not result in appreciable nicking activity (Fig. 7, lane 4). Similarly, nicking of β PKC did not occur in the presence of this concentration of activators with peptide I (lane 9) or with control peptide (lane 8). However, incubation of β PKC with the 30 same concentration of activators in the presence of peptide rVI resulted in a time-dependent appearance of the 78 kDa nicked PKC fragment (Fig. 4, lanes 5-7). Concentrations as low as 10 nM of peptide rVI were sufficient to result in nicking activity, indicative of β PKC activation. The results indicate that peptide 35 rVI, but not peptide I, is effective to stabilize PKC in an activated conformation that renders it susceptible to Arg-C under conditions of low PKC activators that would otherwise not render the enzyme susceptible to Arg-C.

- 57 -

Example 10

Effects of RACK1 WD-40-derived Peptides on PKC Autophosphorylation

Activated PKC is capable of autophosphorylation. peptide rVI (SEQ ID NO:7) was effective to induce PKC translocation and GVBD in the absence of an activator such as insulin, the ability of the peptide to induce PKC autophosphorylation in the absence of PKC activators was assessed.

PKC autophosphorylation in the presence of pseudosubstrate antibodies or the indicated peptides was carried 10 out using a modification of the method described by Makowske, et al. Anti-pseudosubstrate antibodies, which were shown previously to induce autophosphorylation in the absence of PKC activators (Makowske, et al.) were used as a positive control. The results are shown in Figure 8.

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Rat brain PKC (~ 10 nM) was incubated with mild agitation in a final volume of 250 μ l of overlay buffer, as in Example 1 either with anti- β PKC pseudosubstrate antibodies (1:10 dilution, Life Technologies, Gaithersburg, MD) or with the indicated peptide (10 μ M). Where indicated, PS (50 μ g/ml), DG (0.8 μ g/ml) and CaCl₂ (1 mM) were also added. The amount of autophosphorylation was determined after 2 hours for the reaction with the antipseudosubstrate antibodies, or after 15 minutes for the other samples. 50 μ l of a buffer comprised of 20 mM Tris-HCl (pH 7.5), 20 mM MgCl₂, 20 μ M ATP and 5 μ ci/ml [γ -32P]ATP. The mixture was incubated for 15 minutes at room temperature and the reaction was stopped by adding 60 μ l sample buffer (see Example 9). The samples were then boiled for 10 minutes, loaded onto a 10% SDS-PAGE mini gel and electrophoresed. The gel was fixed with 50% methanol and 10% acetic acid for 1 hour, and the autophosphorylation of PKC was determined by autoradiography.

The results in Figure 8 show PKC autophosphorylation in the presence of DG, PS, and calcium (lane 1), in the presence of EGTA (lane 2), in the presence of anti- β PKC pseudosubstrate antibodies (diluted 1:10 in 20 mM Tris-HCl; lane 3), in the presence of peptide rVI (SEQ ID NO:7; 10 μ M; lane 4), in the presence of peptide I (SEQ ID NO:1; 10 μ M; lane 5), or in the presence of control peptide (SEQ ID NO:9; 10 μ M; lane 6).

PCT/US95/01210 WO 95/21252

- 58 -

Peptide rVI in the absence of PKC activators induced PKC autophosphorylation to over 80% of the autophosphorylation obtained in the presence of optimal concentration of PS, DG, and calcium (compare Fig. 8 lane 1 (control) with lane 4 (peptide rVI). control peptide induced I nor 5 Neither peptide autophosphorylation in the absence of PKC activators (Fig. 8 lanes 5 and 6, respectively).

Example 11

Effects of RACK1 WD-40-derived Peptides on Histone Phosphorylation by PKC

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Incubation of PKC with peptide rVI (SEQ ID NO:7) induced histone phosphorylation by PKC. The method used was a modification of the protocol described by Mochly-Rosen, et al. (1987). results are shown in Figure 9.

Histone type IIIs (Sigma Chemical Company, St. Louis, MO) was phosphorylated by PKC (~ 10 nM) in the absence (lane 1) and presence of peptide rVI (10 μ M) (lanes 2 and 3) and in the presence and absence of DG (0.8 μ g/ml), PS (50 μ g/ml) and CaCl₂ (lane 3). The results are expressed as percentage of control that is the amount of Histone phosphorylation by PKC in the presence of DG (0.8 $\mu g/ml$), PS (50 $\mu g/ml$) and CaCl₂ (1 mM). The results are the average ± SEM of two independent experiments. PKC was first incubated with the peptide rVI (10 μ M) for 15 minutes in overlay buffer as described above. Histone type IIIs (40 μ g/ml) was added 25 in Tris-HCl (20 mM), MgCl₂ (20 mM), ATP (20 μ M) and $[\gamma^{-32}P]$ ATP (5 μ ci/ml) with or without PS (50 μ g/ml), DG (0.8 μ g/ml) and CaCl₂ (1 mM). Histone phosphorylation was determined by autoradiography as above.

PKC activators PS, DG, and calcium were not required for peptide rVI-induced autophosphorylation phosphorylation, suggesting that peptide rVI is an agonist of PKC activation.

In a related experiment, phosphorylation of histone type IIIs (25μM) by PKC (10 nM) was not inhibited by RACK1; rather, a 35 4.5±0.1 fold increase of histone phosphorylation occurred when coincubated with ~100 nM RACK1 (n=2).

PCT/US95/01210

- 59 -

WO 95/21252

SEQUENCE LISTING

	(1) GENER	AL INFORMATION:
5	, , ,	approgram Machle Pager Paris
	(1)	APPLICANT: Mochly-Rosen, Daria
		Ron, Dorit
	(ii)	TITLE OF INVENTION: WD-40 - Derived Peptides and Uses
10	\/	Thereof
	(iii)	NUMBER OF SEQUENCES: 265
	(iv)	CORRESPONDENCE ADDRESS:
15		(A) ADDRESSEE: Dehlinger & Associates
		(B) STREET: P.O. Box 60850
		(C) CITY: Palo Alto
		(D) STATE: CA
		(E) COUNTRY: USA
20		(F) ZIP: 94306-0850
	(37)	COMPUTER READABLE FORM:
	()	(A) MEDIUM TYPE: Floppy disk
		(B) COMPUTER: IBM PC compatible
25		(C) OPERATING SYSTEM: PC-DOS/MS-DOS
		(D) SOFTWARE: PatentIn Release #1.0, Version #1.25
		•
	(vi)	CURRENT APPLICATION DATA:
		(A) APPLICATION NUMBER: 08/190,802
30		(B) FILING DATE: 01-FEB-1994
		(C) CLASSIFICATION:
	/*** i i \	ATTORNEY/AGENT INFORMATION:
	(\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	(A) NAME: Fabian, Gary R.
35		(B) REGISTRATION NUMBER: 33,875
		(C) REFERENCE/DOCKET NUMBER: 8600-0139
	(ix)	TELECOMMUNICATION INFORMATION:
		(A) TELEPHONE: (415) 324-0880
40		(B) TELEFAX: (415) 324-0960
	/o\ ====	DESTRUCTION FOR SEC TO NO.1.
	(2) INFO	RMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

PCT/US95/01210

- 60 -

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        (iv) ANTI-SENSE: NO
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(A) LENGTH: 7 amino acids(B) TYPE: amino acid

(D) TOPOLOGY: unknown

PCT/US95/01210 WO 95/21252

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- 61 -
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(A) LENGTH: 7 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

45 (ii) MOLECULE TYPE: peptide - 62 -

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(iii) HYPOTHETICAL: NO
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(iii) HYPOTHETICAL: NO

- 63 -

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(iv) ANTI-SENSE: NO
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(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: Peptide rVI, Fig. 1C

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

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- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

20

15

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Peptide rVII, Fig. 1C
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

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(2) INFORMATION FOR SEQ ID NO:9:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 6 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- .45 (iv) ANTI-SENSE: NO

PCT/US95/01210

- 64 -

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(vi) ORIGINAL SOURCE:
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               (B) TYPE: amino acid
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               (D) TOPOLOGY: unknown
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         (iv) ANTI-SENSE: NO
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                (D) TOPOLOGY: unknown
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          (ii) MOLECULE TYPE: peptide
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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 65 -

(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PKC substrate peptide, (Ser25) PKC(19-36) (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11: Arg Phe Ala Arg Lys Gly Ser Leu Arg Gln Lys Asn Val His Glu Val 10 10 Lys Asn (2) INFORMATION FOR SEQ ID NO:12: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 18 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTAETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PKC Pseudosubstrate Inhibitor (PCK(19-36)) 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12: Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His Glu Val 5 10 35 Lys Asn (2) INFORMATION FOR SEQ ID NO:13: 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids (B) TYPE: amino acid

(D) TOPOLOGY: unknown

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	(iii) HYPOTHETICAL: NO
5	(iv) ANTI-SENSE: NO
•	(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide, rI, Fig. 24
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:
	Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile 1 5 10 15
15	(2) INFORMATION FOR SEQ ID NO:14:
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	(ii) MOLECULE TYPE: peptide
	(iii) HYPOTHETICAL: NO
25	(iv) ANTI-SENSE: NO
	<pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rII, Fig. 24</pre>
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45	(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 67 -

(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rIII, Fig. 24 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15: Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg Gln Ile Val 10 5 10 (2) INFORMATION FOR SEQ ID NO:16: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rIV, Fig. 24 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16: Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser Asn Pro Ile 30 15 10 (2) INFORMATION FOR SEQ ID NO:17: (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 15 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 40 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- 68 -

- (C) INDIVIDUAL ISOLATE: GBH Peptide rV, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17: Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 15 10 (2) INFORMATION FOR SEQ ID NO:18: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 15 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rVI, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18: 25 Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys Phe Ser Pro 10 (2) INFORMATION FOR SEQ ID NO:19: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1115 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double 35 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO 40 (iv) ANTI-SENSE: NO
- 45 (C) INDIVIDUAL ISOLATE: RACK1 DNA Sequence, Fig. 1A

(vi) ORIGINAL SOURCE:

PCT/US95/01210

WO 95/21252

- 69 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

GGCACGAGGG GTCGCGGTGG CAGCCGTGCG GTGCTTGGCT CCCTAAGCTA TCCGGTGCCA

5 TCCTTGTCGC TGCGGCGACT CGCAACATCT GCAGCCATGA CCGAGCAAAT GACCCTTCGT 120 GGGACCCTCA AGGGCCATAA TGGATGGGTT ACACAGATCG CCACCACTCC GCAGTTCCCG 180 GACATGATCC TGTCGGCGTC TCGAGACAAG ACCATCATCA TGTGGAAGCT GACCAGGGAT 240 10 GAGACCAACT ACGGCATACC ACAACGTGCT CTTCGAGGTC ACTCCCACTT TGTTAGCGAT 300 GTTGTCATCT CCTCTGATGG CCAGTTTGCC CTCTCAGGCT CCTGGGATGG AACCCTACGC 360 15 CTCTGGGATC TCACAACGGG CACTACCACG AGACGATTTG TCGGCCACAC CAAGGATGTG CTGAGCGTGG CTTTCTCCTC TGACAACCGG CAGATTGTCT CTGGGTCCCG AGACAAGACC 480 ATTAGGTTAT GGAATACTCT GGGTGTCTGC AAGTACACTG TCCAGGATGA GAGTCATTCA 540 20 GAATGGGTGT CTTGTGTCCG CTTCTCCCCG AACAGCAGCA ACCCTATCAT CGTCTCCTGC 600 GGATGGGACA AGCTGGTCAA GGTGTGGAAT CTGGCTAACT GCAAGCTAAA GACCAACCAC 660 25 ATTGGCCACA CTGGCTATCT GAACACAGTG ACTGTCTCTC CAGATGGATC CCTCTGTGCT 720 TCTGGAGGCA AGGATGGCCA GGCTATGCTG TGGGATCTCA ATGAAGGCAA GCACCTTTAC 780 ACATTAGATG GTGGAGACAT CATCAATGCC TTGTGCTTCA GCCCCAACCG CTACTGGCTC 840 30 TGTGCTGCCA CTGGCCCCAG TATCAAGATC TGGGACTTGG AGGGCAAGAT CATGGTAGAT 900 GAACTGAAGC AAGAAGTTAT CAGCACCAGC AGCAAGGCAG AGCCACCCCA GTGTACCTCT 960 35 1020 TTGGCTTGGT CTGCTGATGG CCAGACTCTG TTTGCTGGCT ATACCGACAA CTTGGTGCGT 1080 GTATGGCAGG TGACTATTGG TACCCGCTAA AAGTTTATGA CAGACTCTTA GAAATAAACT 1115 GGCTTTCTGA AAAAAAAAA AAAAAAAAA AAAAA

(2) INFORMATION FOR SEQ ID NO:20:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 96 base pairs

(B) TYPE: nucleic acid

- 70 -

- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)

5

- (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 10 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rI DNA Sequence, Fig. 1A
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

GGCCATAATG GATGGGTTAC ACAGATCGCC ACCACTCCGC AGTTCCCGGA CATGATCCTG
60

TCGGCGTCTC GAGACAAGAC CATCATCATG TGGAAG

- 20 96
 - (2) INFORMATION FOR SEQ ID NO:21:
 - (i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 94 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- 30 (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

35

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rII DNA Sequence
- 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

GGTCACTCCC ACTTTGTTAG CGATGTTGTC ATCTCCTCTG ATGGCCAGTT TGCCCTCTCA
60

45 GGCTCCTGGG ATGGAACCCT ACGCCTCTGG GATC
94

PCT/US95/01210

- 71 -

- (2) INFORMATION FOR SEQ ID NO:22:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 93 base pairs
 - (B) TYPE: nucleic acid .
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

10

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rIII DNA Sequence, Fig. 1A
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

20

GGCCACACCA AGGATGTGCT GAGCGTGGCT TTCTCCTCTG ACAACCGGCA GATTGTCTCT

GGGTCCCGAG ACAAGACCAT TAAGTTATGG AAT

- 25 93
 - (2) INFORMATION FOR SEQ ID NO:23:
 - (i) SEQUENCE CHARACTERISTICS:

30

- (A) LENGTH: 99 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- 35 (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rIV DNA Sequence, Fig. 1A
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

AGTCATTCAG AATGGGTGTC TTGTGTCCGC TTCTCCCCGA ACAGCAGCAA CCCTATCATC

GTCTCCTGCG GATGGGACAA GCTGGTCAAG GTGTGGAAT

- 5 99
- (2) INFORMATION FOR SEQ ID NO:24:
 - (i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 93 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- 15 (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rV DNA Sequence, Fig. 1A
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

GGCCACACTG GCTATCTGAA CACAGTGACT GTCTCTCCAG ATGGATCCCT CTGTGCTTCT

- 30 GGAGGCAAGG ATGGCCAGGC TATGCTGTGG GAT 93
 - (2) INFORMATION FOR SEQ ID NO:25:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 93 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

- 73 -

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rVI DNA Sequence, Fig. 1A
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

TTAGATGGTG GAGACATCAT CAATGCCTTG TGCTTCAGCC CCAACCGCTA CTGGCTCTGT

- 10 GCTGCCACTG GCCCCAGTAT CAAGATCTGG GAC
 93
 - (2) INFORMATION FOR SEQ ID NO:26:
- . 15 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 99 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

20

- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- 25 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rVII DNA Sequence, Fig. 1A

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

- AGCAAGGCAG AGCCACCCCA GTGTACCTCT TTGGCTTGGT CTGCTGATGG CCAGACTCTG
60

35

TTTGCTGGCT ATACCGACAA CTTGGTGCGT GTATGGCAG
99

(2) INFORMATION FOR SEQ ID NO:27:

40

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

45

(ii) MOLECULE TYPE: protein

PCT/US95/01210

- 74 -

	(iii)	нүро	THET	ICAL	: NO											
	(iv)	ITNA	-SEN	SE:	NO			,								
5	(vi)					ISOL	ATE :	RAC	K1 A	mino	Aci	d Se	dren	ice,	Fig.	1C
10	(xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q II	NO:	27:						
	Met 1	Thr	Glu	Gln	Met 5	Thr	Leu	Arg	Gly	Thr 10	Leu	Lys	Gly	His	Asn 15	Gly
15	Trp	Val	Thr	Gln 20	Ile	Ala	Thr	Thr	Pro 25	Gln	Phe	Pro	Asp	Met 30	Ile	Leu
	Ser	Ala	Ser 35	Arg	Asp	Lys	Thr	Ile 40	Ile	Met	Trp	Lys	Leu 45	Thr	Arg	Asp
20	Glu	Thr 50	Asn	Tyr	Gly	Ile	Pro 55	Gln	Arg	Ala	Leu	Arg 60	Gly	His	Ser	His
	Phe 65	Val	Ser	Asp	Val	Val 70	Ile	Ser	Ser	Asp	Gly 75	Gln	Phe	Ala	Leu	Ser 80
25	Gly	Ser	Trp	Asp	Gly 85	Thr	Leu	Arg	Leu	Trp 90	Asp	Leu	Thr	Thr	Gly 95	Thr
30	Thr	Thr	Arg	Arg 100	Phe	Val	Gly	His	Thr 105	Lys	Asp	Val	Leu	Ser 110	Val	Ala
	Phe	Ser	Ser		Asn	Arg	Gln	Ile 120		Ser	Gly	Ser	Arg 125	Asp	Lys	Thr
35	Ile	Lys 130		Trp	Asn	Thr	Leu 135		Val	Cys	Lys	Tyr 140		Val	Gln	Asp
40	Glu 145		His	Ser	Glu	Trp		Ser	Cys	Val	Arg 155		Ser	Pro	Asn	Ser 160
40	Ser	Asn	Pro) Ile	11e		Ser	Сув	Gly	Trp		Lys	Leu	Val	Lys 175	Val
45	Trp	Asr	ı Lev	1 Ala		Cys	. Lys	Lev	Lys 185		: Asn	His	: Ile	Gly		Thr

- 75 -

Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 205 195 200 Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 215 220 210 5 Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 235 240 225 230 Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 10 255 250 245 Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln 270 265 260 15 Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser 275 280 285 Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp 295 300 290 20 Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg 310 305 25 (2) INFORMATION FOR SEQ ID NO:28: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 501 amino acids (B) TYPE: amino acid 30 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Human 55 kDa protein (PWP homolog), 40 Fig. 11 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Asn Arg Ser Arg Gln Val Thr Cys Val Ala Trp Val Arg Cys Gly

- 76 -

	1				5					10					15	
	Val	Ala	Lys	Glu 20	Thr	Pro	Asp	Lys	Val 25	Glu	Leu	Ser	Lys	Glu 30	Glu	Val
5	Lys	Arg	Leu 35	Ile	Ala	Glu	Ala	Lys 40	Glu	Lys	Leu	Gln	Glu 45	Glu	Gly	Gly
10	Gly	Ser 50	Asp	Glu	Glu	Glu	Thr 55	Gly	Ser	Pro	Ser	Glu 60	Asp	Gly	Met	Gln
	Ser 65	Ala	Arg	Thr	Gln	Ala 70	Arg	Pro	Arg	Glu	Pro 75	Leu	Glu	Asp	Gly	Asp 80
15	Pro	Glu	Asp	Asp	Arg 85	Thr	Leu	Asp	Asp	Asp 90	Glu	Leu	Ala	Glu	Tyr 95	Asp
20	Leu	Asp	Lys	Tyr 100	Asp	Glu	Glu	Gly	Asp 105	Pro	Asp	Ala	Glu	Thr 110	Leu	Gly
20	Glu	Ser	Leu 115	Leu	Gly	Leu	Thr	Val 120	Tyr	Gly	Ser	Asn	Asp 125	Gln	Asp	Pro
25	Tyr	Val 130	Thr	Leu	Lys	Asp	Thr 135	Glu	Gln	Tyr	Glu	Arg 140	Glu	Asp	Phe	Leu
•	Ile 145	Lys	Pro	Ser	Asp	Asn 150	Leu	Ile	Val	Cys	Gly 155	Arg	Ala	Glu	Gln	Asp 160
30	Gln	Сув	Asn	Leu	Glu 165	Val	His	Val	Tyr	Asn 170	Gln	Glu	Glu	Asp	Ser 175	Phe
35	Tyr	Val	His	His 180	Asp	Ile	Leu	Leu	Ser 185		Tyr	Pro	Leu	Ser 190	Val	Glu
	Trp	Leu	Asn 195		Asp	Pro	Ser	Pro 200		Asp	Ser	Thr	Gly 205	Asn	Tyr	Ile
40	Ala	Val 210	Gly	Asn	Met	Thr	Pro 215		Ile	Glu	Val	Trp 220		Leu	Asp	Ile
	Val 225	_	Ser	Leu	Glu	230		Phe	Thr	Leu	Gly 235		Lys	Leu	Ser	Lys 240
45	Lys	Lys	Lys	Lys	Lys	Gly	Lys	Lys	Ser	Ser		Ala	Glu	Gly	His	

- 77 -

٠	Asp	Ala	Val	Leu 260	Asp	Leu	Ser	Trp	Asn 265	Lys	Leu	Ile	Arg	Asn 270	Val	Leu
5	Ala	Ser	Ala 275	Ser	Ala	Asp	Asn	Thr 280	Val	Ile	Leu	Trp	Asp 285	Met	Ser	Leu
	Gly	Lys 290	Pro	Ala	Ala	Ser	Leu 295	Ala	Val	His	Thr	Asp 300	Lys	Val	Gln	Thr
10	Leu 305	Gln	Phe	His	Pro	Phe 310	Glu	Ala	Gln	Thr	Leu 315	Ile	Ser	Gly	Ser	Tyr 320
15	Asp	Lys	Ser	Val	Ala 325	Leu	Tyr	Asp	Cys	Arg 330	Ser	Pro	Asp	Glu	Ser 335	His
15	Arg	Met	Trp	Arg 340	Phe	Ser	Gly	Gln	Ile 345	Glu	Arg	Val	Thr	Trp 350	Asn	His
20	Phe	Ser	Pro 355	Cys	His	Phe	Leu	Ala 360	Ser	Thr	Asp	Asp	365 Gļy	Phe	Val	Tyr
	Asn	Leu 370	Asp	Ala	Arg	Ser	Asp 375	Lys	Pro	Ile	Phe	Thr 380	Leu	Asn	Ala	His
25	Asn 385	Asp	Glu	Ile	Ser	Gly 390	Leu	Asp	Leu	Ser	Ser 395	Gln	Ile	Lys	Gly	Cys 400
30	Leu	Val	Thr	Ala	Ser 405	Ala	qaA	Lys	Tyr	Val 410	Lys	Ile	Trp	Asp	Ile 415	Leu
	Gly	Asp	Arg	Pro 420	Ser	Leu	Val	His	Ser 425	Arg	Asp	Met	Lys	Met 430	Gly	Val
35	Leu	Phe	Cys 435		Ser	Cys	Cys	Pro 440		Leu	Pro	Phe	Ile 445	Tyr	Ala	Phe
	Gly	Gly 450		Lys	Glu	Gly	Leu 455		Val	Trp	Asp	Ile 460	Ser	Thr	Val	Ser
40	Ser 465		Asn	Glu	Ala	Phe 470		Arg	Arg	Glu	Arg 475	Leu	Val	Leu	Gly	Ser 480
45	Ala	Arg	Asn	Ser	Ser 485		Ser	Gly	Pro	Phe 490		Ser	Arg	Ser	Ser 495	Asp
-																

Thr Pro Met Glu Ser

- 78 -

	(2)	INFORM	/ATIC	N FO	R SE	Q ID	NO:	29:									
5		(i) \$	(A) (B)	LENG TYPE TOPO	TH: : an	428 nino	amir acid	no ac									
10 .		(ii) 1					rotei	in									
		(iii) :	HYPO'	THET:	ICAL:	: NO											
15		(iv)	ANTI	-SENS	SE: 1	NO											
		(vi)		INAL IND			ISOL	ATE:	AAC	-RIC	H pr	otei:	n, F	ig.	12		
20		(xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	29:						
		Pro 1	Gly	Gly		Gln 5	His	Leu	Gln		Gln 10	Gln	Gln	Gln	Gln	Gln 15	Gln
25		Gln	Gln		Gln 20	Gln	Gln	Gln	Gln	Gln 25	Gln	Gln	Gln	Thr	Gln 30	Val	Gln
		Gln	Leu	His 35	Asn	Gln	Leu	His	Gln 40	Gln	His	Asn	Gln	Gln 45	Ile	Gln	Gln
30		Gln	Ala 50	Gln	Ala	Thr	Gln	Gln 55	His	Leu	Gln	Thr	Gln 60	Gln	Tyr	Leu	Gln
35		Ser 65	Gln	Ile	His	Gln	Gln 70	Ser	Gln	Gln	Ser	Gln 75	Leu	Ser	Asn	Asn	Leu 80
		Asn	Ser	Asn	Ser	Lys 85	Glu	Ser	Thr	Asn	Ile 90	Pro	Lys	Thr	Asn	Thr 95	Gln
40		Tyr	Thr	Asn	Phe 100		Ser	Lys	Asn	Leu 105		Leu	Ala	Ser	Arg 110		Ph∈
		Sei	Glu	Cys 115		Thr	Lys	Asp	Phe 120		Gly	Asn	Lys	Lys 125		Ser	Thr
45		Set	r Val	Ala	Trp	Asn	Ala	. Asn	Gly	Thr	Lys	Ile	Ala	Ser	Ser	Gly	Se

- 79 -

		130					135					140				
E	Asp 145	Gly	Ile	Val	Arg	Val 150	Trp	Asn	Phe	Asp	Pro 155	Leu	Gly	Asn	Ser	Asn 160
	Asn	Asn	Asn	Asn	Ser 165	Asn	Asn	Thr	Ser	Ser 170	Asn	Ser	Lys	Asn	Asn 175	Asn
10	Ile	Lys	Glu	Thr 180	Ile	Glu	Leu	Lys	Gly 185	His	Asp	Gly	Ser	Ile 190	Glu	Lys
	Ile	Ser	Trp 195	Ser	Pro	Lys	Asn	Asn 200	Asp	Leu	Leu	Ala	Ser 205	Ala	Gly	Thr
15	Asp	Lys 210	Val	Ile	Lys	Ile	Trp 215	Asp	Val	Lys	Ile	Gly 220	Lys	Cys	Ile	Gly
20	Thr 225	Val	Ser	Thr	Asn	Ser 230	Glu	Asn	Ile	Asp	Val 235	-	Trp	Ser	Pro	Asp 240
	Gly	Asp	His	Leu	Ala 245	Leu	Ile	Asp	Leu	Pro 250	Thr	Ile	Lys	Thr	Leu 255	Lys
25	Ile	Tyr	Lys	Phe 260	Asn	Gly	Glu	Glu	Leu 265	Asn	Gln	Val	Gly	Trp 270	Asp	Asn
	Asn	Gly	Asp 275	Leu	Ile	Leu	Met	Ala 280	Asn	Ser	Met	Gly	Asn 285	Ile	Glu	Ala
30	Tyr	Lys 290	Phe	Leu	Pro	Lys	Ser 295	Thr	Thr	His	Val	Lys 300	His	Leu	Lys	Thr
35	Leu 305	Tyr	Gly	His	Thr	Ala 310	Ser	Ile	Tyr	Сув	Met 315	Glu	Phe	Asp	Pro	Thr 320
	Gly	Lys	Tyr	Leu	Ala 325	Ala	Gly	Ser	Ala	Asp 330	Ser	Ile	Val	Ser	Leu 335	Trp
40	Asp	Ile	Glu	Asp 340	Met	Met	Сув	Val	Lys 345	Thr	Phe	Ile	Lys	Ser 350	Thr	Phe
		-	355					360			Gly		365			
45	Ser	Ser 370		Glu	Ser	Thr	1le 375		Ile	Phe	His	Ile 380		Ser	Ser	Gln

- 80 -

Pro Ile His Thr Ile Glu Cys Gly Val Ser Ser Leu Met Trp His Pro 385 390 395 400 Thr Leu Pro Leu Leu Ala Tyr Ala Pro Glu Ser Ile Asn Glu Asn Asn 410 415 405 5 Lys Asp Pro Ser Ile Arg Val Phe Gly Tyr His Ser 425 420 (2) INFORMATION FOR SEQ ID NO:30: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 517 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP, Fig. 13 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30: Met Glu Gly Phe Ser Cys Ser Leu Gln Pro Pro Thr Ala Ser Glu Arg 10 30 Glu Asp Cys Asn Arg Asp Glu Pro Pro Arg Lys Ile Ile Thr Glu Lys 20 25 Asn Thr Leu Arg Gln Thr Lys Leu Ala Asn Gly Thr Ser Ser Met Ile 35 40 45 Val Pro Lys Gln Arg Lys Leu Ser Ala Asn Tyr Glu Lys Glu Lys Glu 55 40 Leu Cys Val Lys Tyr Phe Glu Gln Trp Ser Glu Cys Asp Gln Val Glu 70 Phe Val Glu His Leu Ile Ser Arg Met Cys His Tyr Gln His Gly His 90 45

- 81 -

	Ile	Asn	Thr	Tyr 100	Leu	Lys	Pro	Met	Leu 105	Gln	Arg	Asp	Phe	Ile 110	Thr	Ala
5	Leu	Pro	Ala 115	Arg	Gly	Leu	Asp	His 120	Ile	Ala	Glu	Asn	Ile 125	Leu	Ser	Tyr
•	Leu	Asp 130	Ala	Lys	Ser	Leu	Cys 135	Ser	Ala	Glu	Leu	Val 140	Cys	Lys	Glu	Trp
10	Tyr 145	Arg	Val	Thr	Ser	Asp 150	Gly	Met	Leu	Trp	Lys 155	Lys	Leu	Ile	Glu	Arg 160
15	Met	Val	Arg	Thr	Asp 165	Ser	Leu	Trp	Arg	Gly 170	Leu	Ala	Glu	Arg	Arg 175	Gly
13	Trp	Gly	Gln	Tyr 180	Leu	Phe	Lys	Asn	Lys 185	Pro	Pro	Asp	Gly	Lys 190	Thr	Pro
20	Pro	Asn	Ser 195	Phe	Tyr	Arg	Ala	Leu 200	Tyr	Pro	Lys	Ile	Ile 205	Gln	Asp	Ile
	Glu	Thr 210	Ile	Glu	Ser	Asn	Trp 215	Arg	Cys	Gly	Arg	His 220	Ser	Leu	Gln	Arg
25	Ile 225	His	Cys	Arg	Ser	Glu 230	Thr	Ser	Lys	Gly	Val 235	Tyr	Cys	Leu	Gln	Tyr 240
30	Asp	Asp	Gln	Lys	Ile 245	Val	Ser	Gly	Leu	Arg 250	Asp	Asn	Thr	Ile	Lys 255	Ile
30	Trp	Asp	Lys	Asn 260	Thr	Leu		_	Lys 265	_	Val	Leu	Met	Gly 270	His	Thr
35	Gly	Ser	Val 275	Leu	Cys	Leu	Gln	Tyr 280	Asp	Glu	Arg	Val	Ile 285	Ile	Thr	Gly
	Ser	Asp 290	Ser	Thr	Val	Arg	Val 295	Trp	Asp	Val	Asn	Thr 300	Gly	Glu	Met	Leu
40	Asn 305		Leu	Ile	His	His 310	Cys	Glu	Ala	Val	Leu 315	His	Leu	Arg	Phe	Asn 320
45	Asn	Gly	Met	Met	Val 325		Cys	Ser	Lys	Asp 330	Arg	Ser	Ile	Ala	Val 335	Trp
	Asp	Met	Ala	Ser	Ala	Thr	Asp	Ile	Thr	Leu	Arg	Arg	Val	Leu	Val	Gly

- 81 -

	Ile	Asn	Thr	Туг 100	Leu	Lys	Pro	Met	Leu 105	Gln	Arg	Asp	Phe	Ile 110	Thr	Ala
5	Leu	Pro	Ala 115	Arg	Gly	Leu	Asp	His 120	Ile	Ala	Glu	Asn	Ile 125	Leu	Ser	Tyr
·	Leu	Asp 130	Ala	Lys	Ser	Leu	Cys 135	Ser	Ala	Glu	Leu	Val 140	Cys	Lys	Glu	Trp
10	Tyr 145	Arg	Val	Thr	Ser	Asp 150	Gly	Met	Leu	Trp	Lys 155	Lys	Leu	Ile	Glu	Arg 160
15	Met	Val	Arg	Thr	Asp 165	Ser	Leu	Trp	Arg	Gly 170	Leu	Ala	Glu	Arg	Arg 175	Gly
	Trp	Gly	Gln	Tyr 180	Leu	Phe	Lys	Asn	Lys 185	Pro	Pro	Asp	Gly	Lys 190	Thr	Pro
20	Pro	Asn	Ser 195	Phe	Tyr	Arg	Ala	Leu 200	Tyr	Pro	Lys	Ile	Ile 205	Gln	Asp	Ile
	Glu	Thr 210	Ile	Glu	Ser	Asn	Trp 215	Arg	Cys	Gly	Arg	His 220	Ser	Leu	Gln	Arg
25	Ile 225	His	Cys	Arg	Ser	Glu 230	Thr	Ser	Lys	Gly	Val 235	Tyr	Cys	Leu	Gln	Tyr 240
30	Asp	Asp	Gln	Lys	Ile 245	Val	Ser	Gly	Leu	Arg 250	Asp	Asn	Thr	Ile	Lys 255	Ile
	Trp	Asp	Lys	Asn 260	Thr	Leu	Glu	Cys	Lys 265	Arg	Val	Leu	Met	Gly 270	His	Thr
35	Gly	Ser	Val 275	Leu	Cys	Leu	Gln	Tyr 280	Asp	Glu	Arg	Val	Ile 285	Ile	Thr	Gly
		290				_	295	_				300		Glu		
40	305					310	_ ,				315			Arg		320
45		_			325		-			330				Ala	335	
	Asp	Met	Ala	Ser	Ala	Thr	Asp	Ile	Thr	Leu	Arg	Arg	Val	Leu	Val	Gly

- 82 -

350 345 340 His Arg Ala Ala Val Asn Val Val Asp Phe Asp Asp Lys Tyr Ile Val 360 355 5 Ser Ala Ser Gly Asp Arg Thr Ile Lys Val Trp Asn Thr Ser Thr Cys 375 Glu Phe Val Arg Thr Leu Asn Gly His Lys Arg Gly Ile Ala Cys Leu 390 395 10 Gln Tyr Arg Asp Arg Leu Val Val Ser Gly Ser Ser Asp Asn Thr Ile 405 410 Arg Leu Trp Asp Ile Glu Cys Gly Ala Cys Leu Arg Val Leu Glu Gly . 15 425 420 His Glu Glu Leu Val Arg Cys Ile Arg Phe Asp Asn Lys Arg Ile Val 440 20 Ser Gly Ala Tyr Asp Gly Lys Ile Lys Val Trp Asp Leu Val Ala Ala 455 Leu Asp Pro Arg Ala Pro Ala Gly Thr Leu Cys Leu Arg Thr Leu Val 475 470 25 Glu His Ser Gly Arg Val Phe Arg Leu Gln Phe Asp Glu Phe Gln Ile 485 490 Val Ser Ser Ser His Asp Asp Thr Ile Leu Ile Trp Asp Phe Leu Asn 30 510 505 Asp Pro Gly Leu Ala 515 35 (2) INFORMATION FOR SEQ ID NO:31: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 906 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

	(1V)	ANTI	-SEN	SE:	NO											•
	(vi)		INAL IND			ISOL	ATE:	bet	a-pr	ime-	cop,	Fig	ŗ. 14	ı		
5																
	(xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	31:						
	Met	Pro	Leu	Arg	Leu	Asp	Ile	Lys	Arg	Lys	Leu	Thr	Ala	Arg	Ser	Asp
LO	1				5					10					15	
	Arg	Val	Lys	Ser 20	Val	Asp	Leu	His	Pro 25	Thr	Glu	Pro	Trp	Met 30	Leu	Ala
15	Ser	Leu	Tyr 35	Asn	Gly	Ser	Val	Cys 40	Val	Trp	Asn	His	Glu 45	Thr	Gln	Thr
20	Leu	Val 50	Lys	Thr	Phe	Glu	Val 55	Cys	Asp	Leu	Pro	Val 60	Arg	Ala	Ala	Lys
20	Phe	Val	Ala	Arg	Lys	Asn	Trp	Val	Val	Thr	Gly	Ala	Asp	Asp	Met	Gln
	65					70					75					80
25	Ile	Arg	Val	Phe	Asn 85	Tyr	Asn	Thr	Leu	Glu 90	Arg	Val	His	Met	Phe 95	Glu
•	Ala	His	Ser	Asp 100	Tyr	Ile	Arg	Cys	Ile 105	Ala	Val	His	Pro	Thr 110	Gln	Pro
30	Phe	Ile	Leu 115	Thr	Ser	Ser	Asp	Asp 120	Met	Leu	Ile	Lys	Leu 125	Trp	Asp	Trp
	Asp	Lys 130	Lys	Trp	Ser	Cys	Ser 135	Gln	Val	Phe	Glu	Gly 140	His	Thr	His	Tyr
35	Val	Met	Gln	Ile	Val	Ile	Asn	Pro	Lys	Asp	Asn	Asn	Gln	Phe	Ala	Ser
	145					150					155					160
40	Ala	Ser	Leu	Asp	Arg 165	Thr	Ile	Lys	Val	Trp 170		Leu	Gly	Ser	Ser 175	Ser
	Pro	Asn	Phe	Thr 180		Glu	Gly	His	Glu 185		Gly	Val	Asn	Cys 190		Asp
45	Tyr	Tyr	Ser 195		Gly	Asp	Lys	200		Leu	Ile	Ser	Gly 205		Asp	Asp

- 84 -

	Arg	Leu 210	Val	Lys	Ile	Trp	Asp 215	Tyr	Gln	Asn	Lys	Thr 220	Cys	Val	Gln	Thr
5	Leu 225	Glu	Gly	His	Ala	Gln 230	Asn	Val	Ser	Cys	Ala 235	Ser	Phe	His	Pro	Glu 240
	Leu	Pro	Ile	Ile	Ile 245	Thr	Gly	Ser	Glu	Asp 250	Gly	Thr	Val	Arg	Ile 255	Trp
10	His	Ser	Ser	Thr 260	Tyr	Arg	Leu	Glu	Ser 265	Thr	Leu	Asn	Tyr	Gly 270	Met	Glu
15	Arg	Val	Trp 275	Cys	Val	Ala	Ser	Leu 280	Arg	Gly	Ser	Asn	Asn 285	Val	Ala	Leu
	Gly	Tyr 290	Asp	Glu	Gly	Ser	Ile 295	Ile	Val	Lys	Leu	Gly 300	Arg	Glu	Glu	Pro
20	Ala 305	Met	Ser	Met	Asp	Ala 310	Asn	Gly	Lys	Ile	Ile 315	Trp	Ala	Lys	His	Ser 320
	Glu	Val	Gln	Gln	Ala 325	Asn	Leu	Lys	Ala	Met 330	Gly	Asp	Ala	Glu	Ile 335	Lys
25	Asp	Gly	Glu	Arg 340	Leu	Pro	Leu	Ala	Val 345	Lys	Asp	Met	Gly	Ser 350	Cys	Glu
30	Ile	Tyr	Pro 355	Gln	Thr	Ile	Gln	His 360	Asn	Pro	Asn	Gly	Arg 365	Phe	Val	Val
	Val	Сув 370	Gly	Asp	Gly	Glu	Tyr 3 [.] 75	Ile	Ile	Tyr	Thr	Ala 380	Met	Ala	Leu	Arg
35	Asn 385	Lys	Ser	Phe	Gly	Ser 390	Ala	Gln	Glu	Phe	Ala 395	Trp	Ala	His	Asp	Ser 400
	Ser	Glu	Tyr	Ala	Ile 405	Arg	Glu	Ser	Asn	Ser 410	Val	Val	Lys	Ile	Phe 415	Lys
40	Asn	Phe	Lys	Glu 420	Lys	Lys	Ser	Phe	Lys 425	Pro	Asp	Phe	Gly	Ala 430	Glu	Ser
45	Ile	Tyr	Gly 435	Gly	Phe	Leu	Leu	Gly 440	Val	Arg	Ser	Val	Asn 445	Gly	Leu	Ala
	Dhe	ጥላታተ	Acn	TTT	Glu	Δgn	Thr	Glu	T.e.11	Tle	Δνα	Ara	Tle	Glu	Tle	Gln

- 85 -

		450			٠		455					460				
_	Pro 465	Lys	His	Ile	Phe	Trp 470	Ser	Asp	Ser	Gly	Glu 475	Leu	Val	Cys	Ile	Ala 480
5	Thr	Glu	Glu	Ser	Phe 485	Phe	Ile	Leu	Lys	Tyr 490	Leu	Ser	Glu		Val 495	Leu
10	Ala	Ala	Gln	Glu 500	Thr	His	Glu	Gly	Val 505	Thr	Glu	Asp	Gly	Ile 510	Glu	Asp
	Gly	Phe	Glu 515	Val	Leu	Gly	Glu	Ile 520	Gln	Glu	Ile	Val	Lys 525	Thr	Gly	Leu
15	Trp	Val 530	Gly	Asp	Cys	Phe	Ile 535	Tyr	Thr	Ser	Ser	Val 540	Asn	Arg	Leu	Asn
20	Tyr 545	Tyr	Val	Gly	Gly	Glu 550	Ile	Val	Thr	Ile	Ala 555	His	Leu	Asp	Arg	Thr 560
20	Met	Tyr	Leu	Leu	Gly 565	Tyr	Ile	Pro	Lys	Asp 570	Asn	Arg	Leu	Tyr	Leu 575	
25	Asp	Lys	Glu	Leu 580	Asn	Ile	Val	Ser	Tyr 585	Ser	Leu	Leu	Val	Ser 590	Val	Leu
	Glu	Tyr	Gln 595	Thr	Ala	Val	Met	Arg 600	Arg	Asp	Phe	Ser	Met 605	Ala	Asp	Lys
30	Val	Leu 610	Pro	Thr	Ile	Pro	Lys 615	Glu	Gln	Arg	Thr	Arg 620	Val	Ala	His	Phe
35	Leu 625		Lys	Gln	Gly	Phe 630	Lys	Gln	Gln	Ala	Leu 635	Thr	Val	Ser	Thr	Asp 640
	Pro	Glu	His	Arg	Phe 645	Glu	Leu	Ala	Leu	Gln 650	Leu	Gly	Glu	Leu	Lys 655	Ile
40	Ala	Tyr	Gln	Leu 660		Val	Glu	Ala	Glu 665		Glu	Gln	Lys	Trp 670	Lys	Gln
	Leu	Ala	Glu 675		Ala	Ile	Ser	Lys 680		Pro	Phe	Gly	Leu 685		Gln	Glu
45	Суя	Lev 690		His	Ala	Gln	Asp		Gly	gly	r Leu	Leu 700		Leu	Ala	Thr

- 86 -

		Ala 705	Ser	Gly	Asn	Ala	5er 710	Met	Val	Asn	ГÀЗ	115	Ala	Glu	Gly	Ala	720
5		Arg	Asp	Gly	Lys	Asn 725	Asn	Val	Ala	Phe	Met 730	Ser	Tyr	Phe	Leu	Gln 735	Gly
·		Lys	Leu	Asp	Ala 740	Cys	Leu	Glu	Leu	Leu 745	Ile	Arg	Thr	Gly	Arg 750	Leu	Pro
10		Glu	Ala	Ala 755	Phe	Leu	Ala	Arg	Thr 760	Tyr	Leu	Pro	Ser	Gln 765	Val	Ser	Arg
15		Val	Val 770	Lys	Leu	Trp	Arg	Glu 775	Asn	Leu	Ser	Lys	Val 780	Asn	Gln	Lys	Ala
13		Ala 785	Glu	Ser	Leu	Ala	Asp 790	Pro	Thr	Glu	Tyr	Glu 795	Asn	Leu	Phe	Pro	Gly 800
20		Leu	Lys	Glu	Ala	Phe 805	Val	Val	Glu	Glu	Trp 810	Val	Lys	Glu	Thr	His 815	Ala
		Asp	Leu	Trp	Pro 820	Ala	Lys	Gln	Tyr	Pro 825	Leu	Val	Thr	Pro	Asn 830	Glu	Glu
25		Arg	Asn	Val 835	Met	Glu	Glu	Ala	Lys 840	Gly	Phe	Gln	Pro	Ser 845	Arg	Ser	Ala
30		Ala	Gln 850	Gln	Glu	Leu	Asp	Gly 855	Lys	Pro	Ala	Ser	Pro 860	Thr	Pro	Val	Ile
30		Val 865	Thr	Ser	Gln	Thr	Ala 870	Asn	Lys	Glu	Glu	Lys 875	Ser	Leu	Leu	Glu	Leu 880
35		Glu	Val	Asp	Leu	Asp 885	Asn	Leu	Glu	Ile	Glu 890	Asp	Ile	Asp	Thr	Thr 895	Asp
		Ile	Asn	Leu	Asp 900	Glu	Asp	Ile	Leu	Asp 905	Asp						
40	(2)	INFO	RMAT:	ION	FOR a	SEQ :	ID N	0:32	:								

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid(D) TOPOLOGY: unknown

45 .

(A) LENGTH: 779 amino acids

- 87 -

	(ii)	MOLE	CULE	TYP:	E: p	rote	in		•							
	(iii)	нүро	THET	ICAL	: NO											•
5	(iv)	ANTI	-SEN	SE:	NO											
•	(vi)					ISOL	ATE:	CDC	4 /	CDC2	0 pr	otei	n, F	ig.	15 ,·	
10	(xi)	SEQU	ENCE	DES	CRIP	TION	: SE	Q ID	NO:	32:						
	Met 1	Gly	Ser	Phe	Pro 5	Leu	Ala	Glu	Phe	Pro 10	Leu	Arg	Asp	Ile	Pro 15	Val
15	Pro	Tyr	Ser	Tyr 20	Arg	Val	Ser		Gly 25	Ile	Ala	Ser	Ser	Gly 30	Ser	Val
20	Thr	Ala	Leu 35	Val	Thr	Ala	Ala	Gly 40	Thr	His	Arg	Asn	Ser 45	Ser	Thr	Ala
	Lys	Thr 50	Val	Glu	Thr	Glu	Asp 55	Gly	Glu	Glu	Asp	Ile 60	Asp	Glu	Tyr	Gln
25	Arg 65	Lys	Arg	Ala	Ala	Gly 70	Ser	Gly	Glu	Ser	Thr 75	Pro	Glu	Arg	Ser	Asp
	Phe	Lys	Arg	Val	Lys 85	His	Asp	Asn	His	Lys 90	Thr	Leu	His	Pro	Val 95	Asn
30	Leu	Gln	Asn	Thr 100	Gly	Ala	Ala	Ser	Val 105	Asp	Asn	Asp	Gly	Leu 110	His	Asn
35	Leu		Asp 115	Ile	Ser	Asn	Asp	Ala 120	Glu	Lys	Leu	Leu	Met 125	Ser	Val	Asp
	Asp	Gly 130		Ala	Ala	Pro	Ser 135	Thr	Leu	Ser	Val	Asn 140	Met	Gly	Val	Ala
40	Ser 145		Asn	Val	Ala	Ala 150	Pro	Thr	Thr	Val	Asn 155	Ala	Ala	Thr	Ile	Thr 160
	Gly	Ser	Asp	Val	Ser 165		Asn	Val	Asn	Ser 170		Thr	Ile	Asn	Asn 175	Pro
45	Met	: Glu	ı Glu	. Gly	Ala	Leu	Pro	Leu	Ser	Pro	Thr	Ala	Ser	Ser	Pro	Gly

- 88 -

				180					185					190		
5	Thr	Thr	Thr 195	Pro	Leu	Ala	Lys	Thr 200	Thr	Lys	Thr	Ile	Asn 205	Asn	Asn	Asn
	Asn	Ile 210	Ala	Asp	Leu	Ile	Glu 215	Ser	Lys	Asp	Ser	Ile 220	Ile	Ser	Pro	Glu
10	Tyr 225	Leu	Ser	Asp	Glu	Ile 230	Phe	Ser	Ala	Ile	Asn 235	Asn	Asn	Leu	Pro	His 240
	Ala	Tyr	Phe	Lys	Asn 245	Leu	Leu	Phe	Arg	Leu 250	Val	Ala	Asn	Met	Asp 255	Arg
15	Ser	Glu	Leu	Ser 260	Ąsp	Leu	Gly	Thr	Leu 265	Ile	Lys	Asp	Asn	Leu 270	Lys	Arg
20	Asp	Leu	Ile 275	Thr	Ser	Leu	Pro	Phe 280	Glu	Ile	Ser	Leu	Lys 285	Ile	Phe	Asn
-	Tyr	Leu 290	Gln	Phe	Glu	Asp	Ile 295	Ile	Asn	Ser	Leu	Gly 300	Val	Ser	Gln	Asn
25	Trp 305	Asn	Lys	Ile	Ile	Arg 310	Lys	Ser	Thr	Ser	Leu 315	Trp	Lys	Lys	Leu	Leu 320
	Ile	Ser	Glu	Asn	Phe 325	V al	Ser	Pro	Lys	Gly 330	Phe	Asn	Ser	Leu	Asn 335	Leu
30	Lys	Leu	Ser	Gln 340	Lys	Tyr	Pro	Lys	Leu 345	Ser	Gln	Gln	Asp	Arg 350	Leu	Arg
35	Leu	Ser	Phe 355	Leu	Glu	Asn	Ile	Phe 360	Ile	Leu	Lys	Asn	Trp 365	Tyr	Asn	Pro
	Lys	Phe 370	Val	Pro	Gln	Arg	Thr 375	Thr	Leu	Arg	Gly	His 380	Met	Thr	Ser	Val
40	Ile 385	Thr	Сув	Leu	Gln	Phe 390	Glu	Asp	Asn	Tyr	Val 395	Ile	Thr	Gly	Ala	Asp 400
	Asp	Lys	Met	Ile	Arg 405	Val	Tyr	Asp	Ser	Ile 410	Asn	Lys	Lys	Phe	Leu 415	Leu
45	Gln	Leu	Ser	Gly		Asp	Gly		Val		Ala	Leu	Lys	Tyr 430		His

- 89 -

	Gly	Gly	Ile 435	Leu	Val	Ser	Gly	Ser 440	Thr	Asp	Arg	Thr	Val 445	Arg	Val	Trp
5	Asp	Ile 450	Lys	Lys	Gly	Cys	Cys 455	Thr	His	Val	Phe	Glu 460	Gly	His	Asn	Ser
•	Thr 465	Val	Arg	Cys	Leu	Asp 470	Ile	Val	Glu	Tyr	Lys 475	Asn	Ile	Lys	Tyr	Ile 480
10	Val	Thr	Gly	Ser	Arg 485	Asp	Asn	Thr	Leu	His 490	Val	Trp	Lys	Leu	Pro 495	Lys
15	Glu	Ser	Ser	Val 500	Pro	Asp	His	Gly	Glu 505	Glu	His	Asp	Tyr	Pro 510	Leu	Val
	Phe	His	Thr 515	Pro	Glu	Glu	Asn	Pro 520	Tyr	Phe	Val	Gly	Val 525	Leu	Arg	Gly
20	His	Met 530	Ala	Ser	Val	Arg	Thr 535	Val	Ser	Gly	His	Gly 540	Asn	Ile	Val	Val
	Ser 545	Gly	Ser	Tyr	Asp	Asn 550	Thr	Leu	Ile	Val	Trp 555	Asp	Val	Ala	Gln	Met 560
25	Lys	Cys	Leu	Tyr	Ile 565	Leu	Ser	Gly	His	Thr 570	Asp	Arg	Ile	Tyr	Ser 575	Thr
30	Ile	Tyr	Asp	His 580	Glu	Arg	Lys	Arg	Cys 585	Ile	Ser	Ala	Ser	Met 590	Asp	Thr
	Thr	Ile	Arg 595	Ile	Trp	Asp	Leu	Glu 600	Asn	Ile	Trp	Asn	Asri 605	Gly	Glu	Cys
35	Ser	Tyr 610	Ala	Thr	Asn	Ser	Ala 615	Ser	Pro	Cys	Ala	Lys 620	Ile	Leu	Gly	Ala
	Met 625	Tyr	Thr	Leu	Gln	Gly 630	His	Thr	Ala	Leu	Val 635	Gly	Leu	Leu	Arg	Leu 640
40	Ser	Asp	Lys	Phe	Leu 645	Val	Ser	Ala	Ala	Ala 650	Asp	Gly	Ser	Ile	Arg 655	Gly
45	Trp	Asp	Ala	Asn 660	_	Tyr	Ser	Arg	Lys 665		Ser	Tyr	His	His 670	Thr	Asn
45	Leu	Ser	Ala	Ile	Thr	Thr	Phe	Tyr	Val	Ser	Asp	Asn	Ile	Leu	Val	Ser

- 90 -

680 . 685 675 Gly Ser Glu Asn Gln Phe Asn Ile Tyr Asn Leu Arg Ser Gly Lys Leu 700 695 690 5 Val His Ala Asn Ile Leu Lys Asp Ala Asp Gln Ile Trp Ser Val Asn 720 705 710 Phe Lys Gly Lys Thr Leu Val Ala Ala Val Glu Lys Asp Gly Gln Ser 725 10 Phe Leu Glu Ile Leu Asp Phe Ser Lys Ala Ser Lys Ile Asn Tyr Val 750 740 Ser Asn Pro Val Asn Ser Ser Ser Ser Ser Leu Glu Ser Ile Ser Thr 15 765 755 Ser Leu Gly Leu Thr Arg Thr Thr Ile Ile Pro 770 775 20 (2) INFORMATION FOR SEQ ID NO:33: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 318 amino acids (B) TYPE: amino acid 25 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG, Fig. 16 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:33: Met Ala Glu Thr Leu Thr Leu Arg Ala Thr Leu Lys Gly His Thr Asn 40 5 10 15 Trp Val Thr Ala Ile Ala Thr Pro Leu Asp Pro Ser Ser Asn Thr Leu 20 25 30 45

Leu Ser Ala Ser Arg Asp Lys Ser Val Leu Val Trp Glu Leu Glu Arg

- 91 -

			35					40					45			
5	Ser	Glu 50	Ser	Asn	Tyr	Gly	Tyr 55	Ala	Arg	Lys	Ala	Leu 60	Arg	Gly	His	Ser
	His 65	Phe	Val	Gln	Asp	Val 70	Val	Ile	Ser	Ser	Asp 75	Gly	Gln	Phe	Cys	Leu 80
10	Thr	Gly	Ser	Trp	Asp 85	Gly	Thr	Leu	Arg	Leu 90	Trp	Asp	Leu	Asn	Thr 95	Gly
	Thr	Thr	Thr	Arg 100	Arg	Phe	Val	Gly	His 105	Thr	Lys	Asp	Val	Leu 110	Ser	Val
15	Ala	Phe	Ser 115	Val	Asp	Asn	Arg	Gln 120	Ile	Val	Ser	Gly	Ser 125	Arg	Asp	Lys
20	Thr	Ile 130	Lys	Leu	Trp	Asn	Thr 135	Leu	Gly	Glu	Cys	Lys 140	Tyr	Thr	Ile	Gly
	Glu 145	Pro	Glu	Gly	His	Thr 150	Glu	Trp	Val	Ser	Cys 155	Val	Arg	Phe	Ser	Pro 160
25	Met	Thr	Thr	Asn	Pro 165	Ile	Ile	Val	Ser	Gly 170	Gly	Trp	Asp	Lys	Met 175	Val
	Lys	Val	Trp	Asn 180	Leu	Thr	Asn	Cys	Lys 185	Leu	Lys	Asn	Asn	Leu 190	Val	Gly
30	His	His	Gly 195	Tyr	Val	Asn	Thr	Val 200	Thr	Val	Ser	Pro	Asp 205	Gly	Ser	Leu
35	Cys	Ala 210	Ser	Gly	Gly	Lys	Asp 215	Gly	Ile	Ala	Met	Leu 220	Trp	Asp	Leu	Ala
	Glu 225	Gly	Lys	Arg	Leu	Tyr 230	Ser	Leu	Asp	Ala	Gly 235	Asp	Val	Ile	His	Cys 240
40	Leu	Cys	Phe	Ser	Pro 245		Arg	Tyr	Trp	Leu 250		Ala	Ala	Thr	Gln 255	Ser
	Ser	Ile	Lys	Ile 260		Asp	Leu	Glu	Ser 265		Ser	Ile	Val	Asp 270	Asp	Leu
45	Arg	Pro	Glu 275		Asn	Ile	Thr	Ser 280		Lys	Ala	Gln	Val 285		Tyr	Cys

- 92 -Val Ser Leu Ala Trp Ser Ala Asp Gly Ser Thr Leu Tyr Ser Gly Tyr 290 295 300 Thr Asp Gly Gln Ile Arg Val Trp Ala Val Gly His Ser Leu 315 305 310 5 (2) INFORMATION FOR SEQ ID NO:34: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 658 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 20 (C) INDIVIDUAL ISOLATE: cop-1 protein, Fig. 17 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34: 25 Met Glu Glu Ile Ser Thr Asp Pro Val Val Pro Ala Val Lys Pro Asp 10 Pro Arg Thr Ser Ser Val Gly Glu Gly Ala Asn Arg His Glu Asn Asp 25 20 30 Asp Gly Gly Ser Gly Ser Glu Ile Gly Ala Pro Asp Leu Asp Lys 40 35 Asp Leu Cys Pro Ile Cys Met Gln Ile Ile Lys Asp Ala Phe Leu 35 60 55 Thr Ala Cys Gly His Ser Phe Cys Tyr Met Cys Ile Ile Thr His Leu 70 75 40

Gln Leu Tyr Pro Asn Phe Leu Leu Asp Lys Leu Leu Lys Lys Thr Ser
· 100 105 110

45

Arg Asn Lys Ser Asp Cys Pro Cys Cys Ser Gln His Leu Thr Asn Asn

	Ala	Arg	His 115	Val	Ser	Lys	Thr	Ala 120	Ser	Pro	Leu	Asp	Gln 125	Phe	Arg	Glu
5	Ala	Leu 130	Gln	Arg	Gly	Cys	Asp 135	Val	Ser	Ile	Lys	Glu 140	Val	Asp	Asn	Leu
• •	Leu 145	Thr	Leu	Leu	Ala	Glu 150	Arg	Lys	Arg	Lys	Met 155	Glu	Gln	Glu	Glu	Ala
10	Glu	Arg	Asn	Met	Gln 165	Ile	Leu	Leu	Asp	Phe 170	Leu	His	Cys	Leu	Arg 175	
1 5	Gln	Lys	Val	Asp 180	Glu	Leu	Asn	Glu	Val 185	Gln	Thr	Asp	Leu	Gln 190	Tyr	Ile
15	Lys	Glu	Asp 195	Ile	Asn	Ala	Val	Glu 200	Arg	His	Arg	Ile	Asp 205	Leu	Tyr	Arg
20	Ala	Arg 210	Asp	Arg	Tyr	Ser	Val 215	Lys	Leu	Arg	Met	Leu 220	Gly	Asp	Asp	Pro
	Ser 225	Thr	Arg	Asn	Ala	Trp 230	Pro	His	Glu	Lys	Asn 235	Gln	Ile	Gly	Phe	Asn 24(
25	Ser	Asn	Ser	Leu	Ser 245	Ile	Arg	Gly	Gly	Asn 250	Phe	Val	Gly	Asn	Tyr 255	Gln
30	Asn	Lys	Lys	Val 260	Glu	Gly	Lys	Ala	Gln 265	Gly	Ser	Ser	His	Gly 270	Leu	Pro
30	Lys	Lys	Asp 275	Ala	Leu	Ser	Gly	Ser 280	Asp	Ser	Gln	Ser	Leu 285	Asn	Gln	Ser
35	Thr	Val 290	Ser	Met	Ala	Arg	Lys 295	Lys	Arg	Ile	His	Ala 300	Gln	Phe	Asn	Asp
	Leu 305		Glu	Cys	Tyr	Leu 310	Gln	Lys	Arg	Arg	Gln 315	Leu	Ala	Asp	Gln	Pro
40	Asn	Ser	Lys	Gln	Glu 325	Asn	Asp	Lys	Ser	Val 330	Val	Arg	Arg	Glu	Gly 335	Тух
4.5	Ser	Asn	Gly	Leu 340		Asp	Phe	Gln	Ser 345		Leu	Thr	Thr	Phe 350	Thr	Arg
45	Тут	: Ser	Arg	Leu	Arg	Val	Ile	Ala	Glu	Ile	Arg	His	Gly	Asp	Ile	Phe

- 94 -

			355				•	360					365			
_	His	Ser 370	Ala	Asn	Ile	Val	Ser 375	Ser	Ile	Glu	Phe	Asp 380	Arg	Asp	Asp	Glu
5	Leu 385	Phe	Ala	Thr	Ala	Gly 390	Val	Ser	Arg	Cys	Ile 395	Lys	Val	Phe	Asp	Phe 400
10	Ser	Ser	Val	Val	Asn 405	Glu	Pro	Ala	Asp	Met 41 0	Gln	Cys	Pro	Ile	Val 415	Glu
	Met	Ser	Thr	Arg 420	Ser	Lys	Leu	Ser	Cys 425	Leu	Ser	Trp	Asn	Lys 430	His	Glu
15	Lys	Asn	His 435	Ile	Ala	Ser	Ser	Asp 440	Tyr	Glu	Gly	Ile	Val 445	Thr	Val	Trp
20	Asp	Val 450	Thr	Thr	Arg	Gln	Ser 455	Leu	Met	Glu	Thr	Glu 460	Glu	Asn	Glu	Lys
	Arg 465	Ala	Trp	Ser	Val	Asp 470	Phe	Ser	Arg	Thr	Glu 475	Pro	Ser	Met	Leu	Val 480
25	Ser	Gly	Ser	Asp	Asp 485	Cys	Lys	Val	Lys	Val 490	Trp	Cys	Thr	Arg	Gln 495	Glu
	Ala	Ser	Val	Ile 500	Asn	Ile	Asp	Met	Lys 505	Ala	Asn	Ile	Cys	Cys 510	Val	Lys
30	Tyr	Asn	Pro 515	Gly	Ser	Ser	Asn	Tyr 520	Ile	Ala	Val	Gly	Ser 525	Ala	Asp	His
35	His	Ile 530	His	Tyr	Tyr	Asp	Leu 535	Arg	Asn	Ile	Ser	Gln 540	Pro	Leu	His	Val
	Phe 545		Gly	His	Lys	Lys 550	Ala	Val	Ser	Tyr	Met 555	Lys	Phe	Leu	Ser	Asn 560
40	Asn	Glu	Leu	Ala	Ser 565	Ala	Ser	Thr	Asp	Ser 570	Thr	Leu	Arg	Leu	Trp 575	Asp
	Val	Lys	Asp	Asn 580		Pro	Val	Arg	Thr 585		Arg	Gly	His	Thr 590	Asn	Glu
45	Lys	Asn	Phe 595		Gly	Leu	Thr	Val 600		Ser	Glu	Tyr	Leu 605	Ala	Cys	Gly

- 95 **-**

Ser Glu Thr Thr Arg Tyr Val Tyr His Lys Glu Ile Thr Arg Pro Val 620 610 615 Thr Ser His Arg Phe Gly Ser Pro Asp Met Asp Asp Ala Glu Lys Arg 630 635 625 5 Gln Val Pro Thr Leu Leu Val Arg Phe Ala Gly Arg Val Ile Val Pro 650 655 645 10 Arg Cys (2) INFORMATION FOR SEQ ID NO:35: (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 440 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CORO PROTEIN, Fig. 18 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35: 30 Met Ser Lys Val Val Arg Ser Ser Lys Tyr Arg His Val Phe Ala Ala Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn Leu Lys Thr Lys Ser Ala 35 25 Val Trp Asp Ser Asn Tyr Val Ala Ala Asn Thr Arg Tyr Ile Trp Asp 40 40 Ala Ala Gly Gly Gly Ser Phe Ala Val Glu Ala Ile Pro His Ser Gly 55 Lys Thr Thr Ser Val Pro Leu Phe Asn Gly His Lys Ser Ala Val Leu 70 75 45

- 96 -

	Asp	Ile	Ala	Phe	His 85	Pro	Phe	Asn	Glu	Asn 90	Leu	Val	Gly	Ser	Val 95	Ser
5	Glu	Asp	Cys	Asn 100	Ile	Cys	Ile	Trp	Gly 105	Ile	Pro	Glu	Gly	Gly 110	Leu	Thr
	Asp	Ser	Ile 115	Ser	Thr	Pro	Leu	Gln 120	Thr	Leu	Ser	Gly	His 125	Lys	Arg	Lys
10	Val	Gly 130	Thr	Ile	Ser	Phe	Gly 135	Pro	Val	Ala	Asp	Asn 140	Val	Ala	Val	Thr
	Ser 145	Ser	Gly	Asp	Phe	Leu 150	Val	Lys	Thr	Trp	Asp 155	Val	Glu	Gln	Gly	Lys 160
	Asn	Leu	Thr	Thr	Val 165	Glu	Gly	His	Ser	Asp 170	Met	Ile	Thr	Ser	Cys 175	Glu
20	His	Asn	Gly	Ser 180	Gln	Ile	Val	Thr	Thr 185	Cys	Lys	Asp	Lys	Lys 190	Ala	Arg
	Val	Phe	Asp 195	Pro	Arg	Thr	Asn	Ser 200	Ile	Val	Asn	Glu	Val 205	Val	Cys	His
25	Gln	Gly 210		Lys	Asn	Ser	Arg 215	Ala	Ile	Phe	Ala	Lys 220	Asp	Lys	Val	Ile
	Thr 225		Gly	Phe	Ser	Lys 230	Thr	Ser	Glu	Arg	Glu 235	Leu	His	Ile	Tyr	Asp 240
30	Pro	Arg	Ala	Phe	Thr 245	Thr	Pro	Leu	Ser	Ala 250	Gln	Val	Val	Asp	Ser 255	Ala
35	Ser	Gly	Leu	Leu 260	Met	Pro	Phe	Tyr	Asp 265		Asp	Asn	Ser	Ile 270		Туг
	Leu	ı Ala	Gly 275	_	Gly	Asp	Gly	Asn 280		Arg	Tyr	Tyr	Glu 285		Val	Asp
40	Glu	290		Туг	lle	His	Phe 295		Ser	Glu	Phe	Lys		Ala	Thr	Pro
	Glr 305		g Gly	Let	ı Cys	Phe		Pro	Lys	Arg	Cys 315		Asn	Thr	· Ser	Gl1
45	Cvs	s Glı	ı Ile	. Ala	a Arg	Glv	. Leu	Lys	: Val	Thr	Pro	Phe	Thr	Val	Glu	Pr

- 97 -

330 335 325 Ile Ser Phe Arg Val Pro Arg Lys Ser Asp Ile Phe Gln Gly Asp Ile 340 5 Tyr Pro Asp Thr Tyr Ala Gly Glu Pro Ser Leu Thr Ala Glu Gln Trp 360 355 Val Ser Gly Thr Asn Ala Glu Pro Lys Thr Val Ser Leu Ala Gly Gly 375 10 Phe Val Lys Lys Ala Ser Ala Val Glu Phe Lys Pro Val Val Gln Val 395 390 Gln Glu Gly Pro Lys Asn Glu Lys Glu Leu Arg Glu Glu Tyr Glu Lys 15 410 405 Leu Lys Ile Arg Val Ala Tyr Leu Glu Ser Glu Ile Val Lys Lys Asp 425 420 20 Ala Lys Ile Lys Glu Leu Thr Asn 440 435 (2) INFORMATION FOR SEQ ID NO:36: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 445 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Coronin (p55), Fig. 19 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36: Met Ser Lys Val Val Arg Ser Ser Lys Tyr Arg His Val Phe Ala Ala 10 5 45 Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn Leu Lys Val Thr Lys Ser

- 98 **-**

				20					25					30		
	Ala	Trp	Asp 35	Ser	Asn	Tyr	Val	Ala 40	Ala	Asn	Thr	Arg	Tyr 45	Phe	Gly	Val
5	Ile	Trp 50	Asp	Ala	Ala	Gly	Gly 55	Gly	Ser	Phe	Ala	Val 60	Ile	Pro	His	Glu
10	Ala 65	Ser	Gly	Lys	Thr	Thr 70	Ser	Val	Pro	Leu	Phe 75	Asn	Gly	His	Lys	Ser 80
	Ala	Val	Leu	Asp	Ile 85	Ala	Phe	His	Pro	Phe 90	Asn	Glu	Asn	Leu	Val 95	Gly
15	Ser	Val	Ser	Glu 100	Asp	Cys	Asn	Ile	Cys 105	Ile	Trp	Gly	Ile	Pro 110	Glu	Gly
	Gly	Leu	Thr 115	Asp	Ser	Ile	Ser	Thr 120	Pro	Leu	Gln	Thr	Leu 125	Ser	Gly	His
20	Lys	Arg 130	Lys	Val	Gly	Thr	Ile 135	Ser	Phe	Gly	Pro	Val 140	Ala	Asp	Asn	Val
25	Ala 145		Thr	Ser	Ser	Gly 150	Asp	Phe	Leu	Val	Lys 155	Thr	Trp	Asp	Val	Glu 160
	Gln	Gly	Lys	Asn	Leu 165		Thr	Val	Glu	Gly 170	His	Ser	Asp	Met	Ile 175	Thr
30	Ser	Cys	Glu	Trp 180		His	Asn	Gly	Ser 185	Gln	Ile	Val	Thr	Thr 190	Cys	Lys
3 5	Asp	Lys	Lys 195		Arg	Val	Phe	Asp 200		Arg	Thr	Asn	Ser 205		Val	Asr
33	Glu	Val 210		Cys	His	Gln	Gly 215	Val	Lys	Asn	Ser	Arg 220		Ile	Phe	Ala
40	Lys 225	_	Lys	Val	Ile	230		. Gly	Phe	Ser	Lys 235		Ser	Glu	Arg	Gl: 240
	Lev	ı His	; Ile	туг	245		Arg	, Ala	Phe	250		Pro	Leu	Ser	Ala 255	
45	Val	l Vai	l Asp	Sez 260		a Ser	Gly	Let	1 Lev		. Pro	Phe	тут	270		As

- 99 -

	Asn	Ser	Ile 275		Tyr	Lėu	Ala	Gly 280	Lys	Gly	Asp	Gly	Asn 285	Ile	Arg	Tyr
5	Tyr	Glu 290	Leu	Val	Asp	Glu	Ser 295	Pro	Tyr	Ile	His	Phe 300	Leu	Ser	Glu	Phe
	Lys 305	Ser	Ala	Thr	Pro	Gln 310	Arg	Gly	Leu	Cys	Phe 315	Leu	Pro	Lys	Arg	Cys 320
10	Leu	Asn	Thr	Ser	Glu 325	Cys	Glu	Ile	Ala	Arg 330	Gly	Leu	Lys	Val	Thr 335	Pro
	Phe	Thr	Val	Glu 340	Pro	Ile	Ser	Phe	Arg 345	Val	Pro	Arg	Lys	Ser 350	Asp	Ile
15	Phe	Gln	Gly 355	Asp	Ile	Tyr	Pro	Asp 360	Thr	Tyr	Ala	Gly	Glu 365	Pro	Ser	Leu
20	Thr	Ala 370	Glu	Gln	Trp	Val	Ser 375	Gly	Thr	Asn	Ala	Glu 380	Pro	Lys	Thr	Val
	Ser 385	Leu	Ala	Gly	Gly	Phe 390	Val	Lys	Lys	Ala	Ser 395	Ala	Val	Glu	Phe	Lys 400
25	Pro	Val	Val	Gln	Val 405	Gln	Glu	Gly	Pro	Lys 410	Asn	Glu	Lys	Glu	Leu 415	Arg
30	Glu	Glu	Tyr	Glu 420	Lys	Leu	Lys	Ile	Arg 425	Val	Ala	Tyr	Leu	Glu 430	Ser	Glu
30	Ile	Val	Lys 435	_	Asp	Ala	Lys	Ile 440	Lys	Glu	Leu	Thr	Asn 445			
35	(2) INFO	RMAT	ION	FOR	SEQ	ID N	0:37	:								
	(i)	,) LE	E CH NGTH PE:	: 43	1 am	ino		s				٠			
40		(D) TO	POLO	GY:	unkn	own									
40	(ii)	MOL	ECUL	E TY	PE:	prot	ein									
	(iii)	НХЕ	POTHE	TICA	L: N	10										
45	(iv)	ANT	:I-SE	ense :	NO											

- 100 -

(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa, Fig. 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37: Met Tyr Arg Thr Lys Val Gly Leu Lys Asp Arg Gln Gln Leu Tyr Lys Leu Ile Ile Ser Gln Leu Leu Tyr Asp Gly Tyr Ile Ser Ile Ala Asn Gly Leu Ile Asn Glu Ile Lys Pro Gln Ser Val Cys Ala Pro Ser Glu Gln Leu Leu His Leu Ile Lys Leu Gly Met Glu Asn Asp Asp Thr Ala Val Gln Tyr Ala Ile Gly Arg Ser Asp Thr Val Ala Pro Gly Thr Gly Ile Asp Leu Glu Phe Asp Ala Asp Val Gln Thr Met Ser Pro Glu Ala Ser Glu Tyr Glu Thr Cys Tyr Val Thr Ser His Lys Gly Pro Cys Arg Val Ala Thr Tyr Ser Arg Asp Gly Gln Leu Ile Ala Thr Gly Ser Ala Asp Ala Ser Ile Lys Ile Leu Asp Thr Glu Arg Met Leu Ala Lys Ser Ala Met Pro Ile Glu Val Met Met Asn Glu Thr Ala Gln Gln Asn Met Glu Asn His Pro Val Ile Arg Thr Leu Tyr Asp His Val Asp Glu Val Thr Cys Leu Ala Phe His Pro Thr Glu Gln Ile Leu Ala Ser Gly Ser

> Arg Asp Tyr Thr Leu Lys Leu Phe Asp Tyr Ser Lys Pro Ser Ala Lys 195 200 205

Arg Ala Phe Lys Tyr Ile Gln Glu Ala Glu Met Leu Arg Ser Ile Ser

- 101 -

Phe His Pro Ser Gly Asp Phe Ile Leu Val Gly Thr Gln His Pro Thr Leu Arg Leu Tyr Asp Ile Asn Thr Phe Gln Cys Phe Val Ser Cys Asn Pro Gln Asp Gln His Thr Asp Ala Ile Cys Ser Val Asn Tyr Asn Ser Ser Ala Asn Met Tyr Val Thr Gly Ser Lys Asp Gly Cys Ile Lys Leu Trp Asp Gly Val Ser Asn Arg Cys Ile Thr Thr Phe Glu Lys Ala His Asp Gly Ala Glu Val Cys Ser Ala Ile Phe Ser Lys Asn Ser Lys Tyr Ile Leu Ser Ser Gly Lys Asp Ser Val Ala Lys Leu Trp Glu Ile Ser 325 330 Thr Gly Arg Thr Leu Val Arg Tyr Thr Gly Ala Gly Leu Ser Gly Arg Gln Val His Arg Thr Gln Ala Val Phe Asn His Thr Glu Asp Tyr Val Leu Leu Pro Asp Glu Arg Thr Ile Ser Leu Cys Cys Trp Asp Ser Arg Thr Ala Glu Arg Arg Asn Leu Leu Ser Leu Gly His Asn Asn Ile Val Arg Cys Ile Val His Ser Pro Thr Asn Pro Gly Phe Met Thr Cys Ser Asp Asp Phe Arg Ala Arg Phe Trp Tyr Arg Arg Ser Thr Thr Asp

(2) INFORMATION FOR SEQ ID NO:38:

- (i) SEQUENCE CHARACTERISTICS:
- 45 (A) LENGTH: 340 amino acids
 - (B) TYPE: amino acid

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							102									
		(D)	TOF	OLOG	Y: u	nkno	wii									
	(ii)	MOLE	CULE	TYP	E: p	rote	in	٠								
5	(iii)	HYPC	THET	CICAL	ı: NO	•										
	(iv)	ANTI	-sen	ISE:	ио						•					
10	(vi)	ORIG (C)					ATE :	G-E	Beta	1 bc	vine	e, Fi	.g. 2	1		
	(xi)	SEQU	JENCE	E DES	CRIF	OIT	1: SE	EQ II	NO:	:38:						
15	Met 1	Ser	Glu	Leu	Asp 5	Gln	Leu	Arg	Gln	Glu 10	Ala	Glu	Gln	Leu	Lys 15	Asn
20	Gln	Ile	Arg	Asp 20	Ala	Arg	Lys	Ala	Cys 25	Ala	Asp	Ala	Thr	Leu 30	Ser	Gln
20	Ile	Thr	Asn 35	Asn	Ile	Asp	Pro	Val 40	Gly	Arg	Ile	Gln	Met 45	Arg	Thr	Arg
25	Arg	Thr 50	Leu	Arg	Gly	His	Leu 55	Ala	Lys	Ile	Tyr	Ala 60	Met	His	Trp	Gly
	Thr 65	Asp	Ser	Arg	Leu	Leu 70	Val	Ser	Ala	Ser	Gln 75	Asp	Gly	Lys	Leu	Ile 80
30	Ile	Trp	Asp	Ser	Tyr 85	Thr	Thr	Asn	Lys	Val 90	His	Ala	Ile	Pro	Leu 95	Arg
35	Ser	Ser	Trp	Val 100	Met	Thr	Cys	Ala	Tyr 105	Ala	Pro	Ser	Gly	Asn 110	Tyr	Val
35	Ala	Cys	Gly 115	_	Leu	Asp	Asn	Ile 120		Ser	Ile	Tyr	Asn 125	Leu	Lys	Thr
40	Arg	130		Asn	Val	Arg	Val		Arg	Glu	Leu	Ala 140	Gly	His	Thr	Gly
	Ty:	: Leu	Ser	Cys	Cys	Arg		Leu	Asp	Asp	Asn 155		Ile	Val	Thr	Ser 160

Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly Gln Gln

165

170

- 103 -

Thr Thr Thr Phe Thr Gly His Thr Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Thr Arg Leu Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp Val Arg Glu Gly Met Cys Arg Gln Thr Phe Thr Gly His Glu Ser Asp Ile Asn Ala Ile Cys Phe Phe Pro Asn Gly Asn Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Leu Arg Ala Asp Gln Glu Leu Met Thr Tyr Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ser Phe Ser Lys Ser Gly Arg Leu Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Ala Leu Lys Ala Asp Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val . 320 Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn (2) INFORMATION FOR SEQ ID NO:39: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 326 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 104 -

	(vi)		INAL IND				ATE:	G-E	eta-	bov	rine	(2),	Fig	j. 22	.	•
								•					•			
5	(xi)	SEQU	JENCE	DES	CRIP	TION	: SE	Q II	NO:	39:						
	Arg 1	Asn	Gln	Ile	Arg 5	Asp	Ala	Arg	Lys	Ala 10	Cys	Gly	Asp	Ser	Thr 15	Leu
LO	Thr	Gln	Ile	Thr 20	Ala	Gly	Leu	Asp	Pro 25	Val	Gly	Arg	Ile	Gln 30	Met	Arg
15	Thr	Arg	Arg 35	Thr	Leu	Arg	Gly	His 40	Leu	Ala	Lys	Ile	Tyr 45	Ala	Met	His
LJ	Trp	Gly 50	Thr	Asp	Ser	Arg	Leu 55	Leu	Val	Ser	Ala	Ser 60	Gln	Asp	Gly	Lys
20	Leu 65	Ile	Ile	Trp	Asp	Ser 70	Glu	Gly	Asn	Val	Arg 75	Tyr	Thr	Thr	Asn	Lys 80
	Val	His	Ala	Ile	Pro 85	Leu	Arg	Ser	Ser	Trp 90	Val	Met	Thr	Cys	Ala 35	Tyr
25	Ala	Pro	Ser	Gly 100	Asn	Phe	Val	Ala	Cys 105	Gly	Gly	Leu	Asp	Asn 110	Ile	Cys
30	Ser	Ile	Tyr 115	Ser	Leu	Lys	Thr	Arg 120	Val	Ser	Arg	Glu	Leu 125	Pro	Gly	His
	Thr	Gly 130	Tyr	Leu	Ser	Cys	Сув 135	Arg	Phe	Leu	Asp	Asp 140	Asn	Gln	Ile	Ile
35	Thr 145	Ser	Ser	Gly	Asp	Thr 150	Thr	Cys	Ala	Leu	Trp 155	Asp	Ile	Glu	Thr	Gly 160
	Gln	Gln	Thr	Val	Gly 165	Phe	Ala	Gly	His	Ser 170	Gly	Asp	Val	Met	Ser 175	Leu
40	Ser	Leu	Ala	Pro 180	Asp	Gly	Arg	Thr	Phe 185	Val	Ser	Gly	Ala	Суз 190	Asp	Ala
	Ser	Ile	Lys 195		Trp	Asp	Val	Arg 200		Ser	Met	Cys	Arg 205	Gln	Thr	Phe
45	Ile	Gly	His	Glu	Ser	Asp	Ile	Asn	Ala	Val	Ala	Phe	Phe	Pro	Asn	Gly

- 105 -

215 220 210 Tyr Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 5 Leu Arg Ala Asp Gln Glu Leu Leu Met Tyr Ser His Asp Asn Ile Ile 245 Cys Gly Ile Thr Ser Val Ala Phe Ser Arg Ser Gly Arg Leu Leu Leu 265 10 Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile Trp Asp Ala Met Lys Gly 280 Asp Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu 15 295 Gly Val Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser 305 310 315 20 Phe Leu Lys Ile Trp Asn 325 (2) INFORMATION FOR SEQ ID NO:40: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH, Fig. 23 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:40: Met Asn Glu Leu Asp Ser Leu Arg Gln Glu Ala Glu Ser Leu Lys Asn 10 15 45

Ala Ile Arg Asp Ala Arg Lys Ala Ala Cys Asp Thr Ser Leu Leu Gln

- 106 -

				20					25					30		
5	Ala	Ala	Thr 35	Ser	Leu	Glu	Pro	Ile 40	Gly	Arg	Ile	Gln	Met 45	Arg	Thr	Arg
	Arg	Thr 50	Leu	Arg	Gly	His	Leu 55	Ala	Lys	Ile	Tyr	Ala 60	Met	His	Trp	Gly
10 .	Asn 65	Asp	Ser	Arg	Asn	Leu 70	Val	Ser	Ala	Ser	Gln 75	Asp	Gly	Lys	Leu	Ile 80
	Val	Trp	Asp	Ser	His 85	Thr	Thr	Asn	Lys	Val 90	His	Ala	Ile	Pro	Leu 95	Arg
15	Ser	Ser	Trp	Val 100	Met	Thr	Cys	Ala	Tyr 105	Ala	Pro	Ser	Gly	Ser 110	Tyr	Val
20	Ala	Cys	Gly 115	Gly	Leu	Asp	Asn	Met 120	Cys	Ser	Ile	Tyr	Asn 125	Leu	Lys	Thr
	Arg	Glu 130	Gly	Asn	Val	Arg	Val 135	Ser	Arg	Glu	Leu	Pro 140	Gly	His	Gly	Gly
25	Tyr 145	Leu	Ser	Cys	Cys	Arg 150	Phe	Leu	Asp	Asp	Asn 155	Gln	Ile	Val	Thr	Ser 160
	Ser	Gly	Asp	Met	Ser 165	Cys	Gly	Leu	Trp	Asp 170	Ile	Glu	Thr	Gly	Leu 175	Gln
30	Val	Thr	Ser	Phe 180	Leu	Gly	His	Thr	Gly 185	Asp	Val	Met	Ala	Leu 190	Ser	Leu
35	Ala	Pro	Gln 195	Cys	Lys	Thr	Phe	Val 200	Ser	Gly	Ala	Cys	Asp 205	Ala	Ser	Ala
	Lys	Leu 210	Trp	Asp	Ile	Arg	Glu 215	Gly	Val	Cys	Lys	Gln 220	Thr	Phe	Pro	Gly
40	His 225		Ser	Asp	Ile	Asn 230	Ala	Val	Thr	Phe	Phe 235	Pro	Asn	Gly	Gln	Ala 240
	Phe	Ala	Thr	Gly	Ser 245	Asp	Asp	Ala	Thr	Cys 250		Leu	Phe	Asp	Ile 255	Arg
45	Ala	Asp	Gln	Glu 260		Ala	Met	Tyr	Ser		Asp	Asn	Ile	Ile 270	-	Gly

- 107 -

Ile Thr Ser Val Ala Phe Ser Lys Ser Gly Arg Leu Leu Ala Gly 275 280 Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Thr Met Lys Ala Glu Arg 290 5 Ser Gly Ile Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val 315 305 Thr Glu Asn Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu 10 325 330 Arg Val Trp Asn 340 15 (2) INFORMATION FOR SEQ ID NO:41: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 317 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN, Fig. 24 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly 35 Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu 25 40 Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp 40 Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His

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- 108 **-**

	Phe 65	Val	Ser	Asp	Val	Val 70	Ile	Ser	Ser [']	Asp	Gly 75	Gln	Phe	Ala	Leu	Ser 80
5	Gly	Ser	Trp	Asp	Gly 85	Thr	Leu	Arg	Leu	Trp 90	Asp	Leu	Thr	Thr	Gly 95	Thr
	Thr	Thr	Arg	Arg 100	Phe	Val	Gly	His	Thr 105	Lys	Asp	Val	Leu	Ser 110	Val	Ala
10	Phe	Ser	Ser 115	Asp	Asn	Arg	Gln	Ile 120	Val	Ser	Gly	Ser	Arg 125	Asp	Lys	Thr
15	Ile	Lys 130	Leu	Trp	Asn	Thr	Leu 135	Gly	Val	Cys	Lys	Tyr 140	Thr	Val	Gln	Asp
	Glu 145	Ser	His	Ser	Glu	Trp 150	Val	Ser	Cys	Val	Arg 155	Phe	Ser	Pro	Asn	Ser 160
20	Ser	Asn	Pro	Ile	Ile 165	Val	Ser	Cys	Gly	Trp 170	Asp	Lys	Leu	Val	Lys 175	Val
	Trp	Asn	Leu	Ala 180	Asn	Cys	Lys	Leu	Lys 185	Thr	Asn	His	Ile	Gly 190	His	Thr
25	Gly	Tyr	Leu 195	Asn	Thr	Val	Thr	Val 200	Ser	Pro	Asp	Gly	Ser 205	Leu	Cys	Ala
30	Ser	Gly 210	Gly	Lys	Asp	Gly	Gln 215	Ala	Met	Leu	Trp	Asp 220	Leu	Asn	Glu	Gly
	Lys 225	His	Leu	Tyr	Thr	Leu 230		Gly	Gly	Asp	Ile 235		Asn	Ala	Leu	Cys 240 .
35	Phe	Ser	Pro	Asn	Arg 245		Trp	Leu	Cys	Ala 250	Ala	Thr	Gly	Pro	Ser 255	Ile
	Lys	Ile	Trp	Asp 260		Glu	Gly	Lys	Ile 265		Val	Asp	Glu	Leu 270	Lys	Gln
40	Glu	Val	11e 275		Thr	Ser	Ser	Lys 280		Glu	Pro	Pro	Gln 285	Cys	Thr	Ser
45	Leu	Ala 290	_	Ser	Ala	. Asp	Gly 295		Thr	Leu	Phe	Ala 300		Tyr	Thr	Asp
	Asn	Lev	val	Arg	Val	Trp	Gln	Val	Thr	: Ile	Gly	Thr	Arg			

- 109 -

305 310 315 (2) INFORMATION FOR SEQ ID NO:42: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 340 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 10 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 15 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 2 (Human), Fig. 25 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:42: Met Ser Glu Leu Glu Gln Leu Arg Gln Glu Ala Glu Gln Leu Arg Asn 5 10 15 25 Gln Ile Arg Asp Ala Arg Lys Ala Cys Gly Asp Ser Thr Leu Thr Gln 20 Ile Thr Ala Gly Leu Asp Pro Val Gly Arg Ile Gln Met Arg Thr Arg 35 40 30 Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly 50 55 60 Thr Asp Ser Arg Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile 35 70 75 80 Ile Trp Asp Ser Tyr Thr Thr Asn Lys Val His Ala Ile Pro Leu Arg 85 90

> 110 Ala Cys Gly Gly Leu Asp Asn Ile Cys Ser Ile Tyr Ser Leu Lys Thr 115 120 Arg Glu Gly Asn Val Arg Val Ser Arg Glu Leu Pro Gly His Thr Gly

100

Ser Ser Trp Val Met Thr Cys Ala Tyr Ala Pro Ser Gly Asn Phe Val

105

40

- 110 -

Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly Gln Gln Thr Val Gly Phe Ala Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp Val Arg Asp Ser Met Cys Arg Gln Thr Phe Ile Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Leu Arg Ala Asp Gln Glu Leu Leu Met Tyr Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg Ser Gly Arg Leu Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile Trp Asp Ala Met Lys Gly Asp Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn

(2) INFORMATION FOR SEQ ID NO:43:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 29 amino acids
 - (B) TYPE: amino acid

- 111 -

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

5 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

10 (C) INDIVIDUAL ISOLATE: G-Beta 4 (mouse), Fig. 26

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Lys Lys Asx Glu Thr Asx Val Asn Met Gly Arg Tyr Thr Pro Arg Ile
1 5 10 15

Lys His Ile Lys Arg Pro Arg Arg Thr Asp Xaa Xaa Gly
20 25

20

45

- (2) INFORMATION FOR SEQ ID NO:44:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 718 amino acids

25 (B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein
- 30 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 35 (C) INDIVIDUAL ISOLATE: GROUCHO PROTEIN DROSOPH, Fig. 27
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
- Met Tyr Pro Ser Pro Val Arg His Pro Ala Ala Gly Gly Pro Pro Pro 1 5 10 15

Gln Gly Pro Ile Lys Phe Thr Ile Ala Asp Thr Leu Glu Arg Ile Lys
20 25 30

Glu Glu Phe Asn Phe Leu Gln Ala His Tyr His Ser Ile Lys Leu Glu

- 112 -

			35					40					45			
_	Cys	Glu 50	Lys	Leu	Ser	Asn	Glu 55	Lys	Thr	Glu	Met	Gln 60	Arg	His	Tyr	Val
5	Met 65	Tyr	Tyr	Glu	Met	Ser 70	Tyr	Gly	Leu	Asn	Val 75	Glu	Met	His	Lys	Gln 80
10	Thr	Glu	Ile	Ala	Lys 85	Arg	Leu	Asn	Thr	Leu 90	Ile	Asn	Gln	Leu	Leu 95	Pro
	Phe	Leu	Gln	Ala 100	Asp	His	Gln	Gln	Gln 105	Val	Leu	Gln	Ala	Val 110	Glu	Arg
15	Ala	Lys	Gln 115	Val	Thr	Met	Gln	Glu 120	Leu	Asn	Leu		Ile 125	Gly	Gļn	Gln
20	Ile	His 130	Ala	Gln	Gln	Val	Pro 135	Gly	Gly	Pro	Pro	Gln 140	Pro	Met	Gly	Ala
	Leu 145	Asn	Pro	Phe	Gly	Ala 150	Leu	Gly	Ala	Thr	Met 155	Gly	Leu	Pro	His	Gly 160
25	Pro	Gln	Gly	Leu	Leu 165	Asn	Lys	Pro	Pro	Glu 170	His	His	Arg	Pro	Asp 175	Ile
	Lys	Pro	Thr	Gly 180	Leu	Glu	Gly	Pro	Ala 185	Ala	Ala	Glu	Glu	Arg 190	Leu	Arg
30	Asn	Ser	Val 195	Ser	Pro	Ala	Asp	Arg 200	Glu	Lys	Tyr	Arg	Thr 205	Arg	Ser	Pro
35	Leu	Asp 210	Ile	Glu	Asn	Asp	Ser 215	Lys	Arg	Arg	Lys	Asp 220	Glu	Lys	Leu	Gln
	Glu 225	Asp	Glu	Gly	Glu	Lys 230	Ser	Asp	Gln	Asp	Leu 235	Val	Val	Asp	Val	Ala 240
40	Asn	Glu	Met	Glu	Ser 245	His	Ser	Pro	Arg	Pro 250	Asn	Gly	Glu	His	Val 255	Ser
	Met	Glu	Val	Arg 260	Asp	Arg	Glu	Ser	Leu 265	Asn	Gly	Glu	Arg	Leu 270	Glu	Lys
45	Pro	Ser	Ser 275	Ser	Gly	Ile	Lys	Gln 280	Glu	Arg	Pro	Pro	Ser 285	Arg	Ser	Gly

- 113 -

	Ser	Ser 290	Ser	Ser	Arg	Ser	Thr 295	Pro	Ser	Leu	Lys	Thr 300	Lys	Asp	Met	Glu
5	Lys 305	Pro	Gly	Thr	Pro	Gly 310	Ala	Lys	Ala	Arg	Thr 315	Pro	Thr	Pro	Asn	Ala 320
·	Ala	Ala	Pro	Ala	Pro 325	Gly	Val	Asn	Pro	Lys 330	Gln	Met	Met	Pro	Gln 335	Gly
10	Pro	Pro	Pro	Ala 340	Gly	Tyr	Pro	Gly	Ala 345	Pro	Tyr	Gln	Arg	Pro 350	Ala	Asp
15	Pro	Tyr	Gln 355	Arg	Pro	Pro	Ser	Asp 360	Pro	Ala	Tyr	Gly	Arg 365	Pro	Pro	Pro
	Met	Pro 370	Tyr	Asp	Pro	His	Ala 375	His	Val	Arg	Thr	Asn 380	Gly	Ile	Pro	His
20	Pro 385	Ser	Ala	Leu	Thr	Gly 390	Gly	Lys	Pro	Ala	Tyr 395	Ser	Phe	His	Met	Asn 400
	Gly	Glu	Gly	Ser	Leu 405	Gln	Pro	Val	Pro	Phe 410	Pro	Pro	Asp	Ala	Leu 415	Val
25	Gly	Val	Gly	Ile 420	Pro	Arg	His	Ala	Arg 425	Gln	Ile	Asn	Thr	Leu 430	Ser	His
30	Gly	Glu	Val 435	Val	Cys	Ala	Val	Thr 440	Ile	Ser	Asn	Pro	Thr 445	Lys	Tyr-	Val
	Tyr	Thr 450	Gly	Gly	Lys	Gly	Cys 455	Val	Lys	Val	Trp	Asp 460	Ile	Ser	Gln	Pro
35	Gly 465	Asn	Lys	Asn	Pro	Val 470	Ser	Gln	Leu	Asp	Cys 475	Leu	Gln	Arg	Asp	Asn 480
	Tyr	Ile	Arg	Ser	Val 485	Lys	Leu	Leu	Pro	Asp 490	Gly	Arg	Thr	Leu	Ile 495	Val
40	Gly	Gly	Glu	Ala 500	Ser	Asn	Leu	Ser	Ile 505	Trp	Asp	Leu	Ala	Ser 510	Pro	Thr
45	Pro	Arg	Ile 515	Lys	Ala	Glu	Leu	Thr 520	Ser	Ala	Ala	Pro	Ala 525	Сув	Tyr	Ala
	Leu	Ala	Ser	Pro	Asp	Ser	Lys	Val	Cys	Phe	Ser	Cys	Cys	Ser	Asp	Gly

PCT/US95/01210 ₩O 95/21252

- 114 -

Asn Ile Ala Val Trp Asp Leu His Asn Glu Ile Leu Val Arg Gln Phe Gln Gly His Thr Asp Gly Ala Ser Cys Ile Asp Ile Ser Pro Asp Gly Ser Arg Leu Trp Thr Gly Gly Leu Asp Asn Thr Val Arg Ser Trp Asp Leu Arg Glu Gly Arg Gln Leu Gln Gln His Asp Phe Ser Ser Gln Ile Phe Ser Leu Gly Tyr Cys Pro Thr Gly Asp Trp Leu Ala Val Gly Met Glu Asn Ser His Val Glu Val Leu His Ala Ser Lys Pro Asp Lys Tyr Gln Leu His Leu His Glu Ser Cys Val Leu Ser Leu Arg Phe Ala Ala Cys Gly Lys Trp Phe Val Ser Thr Gly Lys Asp Asn Leu Leu Asn Ala Trp Arg Thr Pro Tyr Gly Ala Ser Ile Phe Gln Ser Lys Glu Thr Ser Ser Val Leu Ser Cys Asp Ile Ser Thr Asp Asp Lys Tyr Ile Val Thr Gly Ser Gly Asp Lys Lys Ala Thr Val Tyr Glu Val Ile Tyr (2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 341 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

- 115 -

	(iv)	ANTI	-SEN	ISE:	NO					,						
	(vi)						LATE :	GTI) bir	ndino	pro	oteir	ı (so	uid)	. Fi	ig. 28
5		, -,								•	•			<u>.</u> ,	•	J
. •	(xi)	SEQU	JENCE	E DES	CRIE	PTION	1: SE	EQ II	NO:	45:						
	Met 1	Thr	Ser	Glu	Leu 5	Glu	Ala	Leu	Arg	Gln 10	Glu	Thr	Glu	Gln	Leu 15 '	
10																
	Asn	Gln	Ile	Arg 20	Glu	Ala	Arg	Lys	Ala 25	Ala	Ala	Asp	Thr	Thr 30	Leu	Ala
15	Met	Ala	Thr	Ala	Asn	Val	Glu	Pro	Val	Gly	Arg	Ile	Gln 45	Met	Arg	Thr
													••		٠	
	Arg	Arg 50	Thr	Leu	Arg	Gly	His 55	Leu	Ala	Lys	Ile	Tyr 60	Ala	Met	His	Trp
20	Ala 65	Ser	Asp	Ser	Arg	Asn 70	Leu	Val	Ser	Ala	Ser 75	Gln	Asp	Gly	Lys	Leu 80
	Ile	Val	Trp	Asp	Gly 85	Tyr	Thr	Thr	Asn	Lys 90	Val	His	Ala	Ile	Pro 95	Leu
25	Arg	Ser	Ser	Trp 100	Val	Met	Thr	Cys	Ala 105	Tyr	Ala	Pro	Ser	Gly 110	Asn	Tyr
30	Val	Ala	Cys 115	Gly	Gly	Leu	Asp	Asn 120	Ile	Cys	Ser	Ile	Tyr 125	Ser	Leu	Lys
	Thr	Arg 130	Glu	Gly	Asn	Val	Arg 135		Ser	Arg	Glu-	Leu 140	Pro	Gly	His	Thr .
35	Gly 145	Tyr	Leu	Ser	Суз	Cys 150	Arg	Phe	Ile	Asp	Asp 155	Asn	Gln	Ile	Val	Thr 160
40	Ser	Ser	Gly	Asp	Met 165	Thr	Cys	Ala	Leu	Trp 170	Asn	Ile	Glu	Thr	Gly 175	Asn
40	Gln	Ile	Thr	Ser 180	Phe	Gly	Gly	His	Thr 185	Gly	Asp	Val	Met	Ser 190	Leu	Ser
	Leu	Ala	Pro	Asp	Met	Arg	Thr	Phe	Val	Ser	Gly	Ala	Cys	Asp	Ala	Ser
45			195					200					205			

- 116 -

	Ala	Lys 210	Leu	Phe	Asp	Ile	Arg 215	Asp	Gly	Ile	Cys	Lys 220	Gln	Thr	Phe	Thr
5	Gly 225	His	Glu	Ser	Asp	Ile 230	Asn	Ala	Ile	Thr	Tyr 235	Phe	Pro	Asn	Gly	Phe 240
	Ala	Phe	Ala	Thr	Gly 245	Ser	Asp	Asp	Ala	Thr 250	Cys	Arg	Leu	Phe	Asp 255	Ile
10	Arg	Ala	Asp	Gln 260	Glu	Ile	Gly	Met	Tyr 265	Ser	His	Asp	Asn	Ile 270	Ile	Cys
15	Gly	Ile	Thr 275	Ser	Val	Ala	Phe	Ser 280	Lys	Ser	Gly	Arg	Leu 285	Leu	Leu	Gly
13	Gly	Tyr 290	Asp	Asp	Phe	Asn	Cys 295	Asn	Val	Trp	Asp	Val 300	Leu	Lys	Gln	Glu
20	Arg 305	Ala	Gly	Val	Leu	Ala 310	Gly	His	Asp	Asn	Arg 315	Val	Ser	Cys	Leu	Gly 320
20			~ 3	•	61		31-	37-1	27.0	Wh ex		Cor	There	Nan	Cor	Dhe
	Val	Thr	GIU	Asp	325	Met	Ala	Val	ALG	330	GIY	per	iip	Asp	335	FIIC
25	Leu	Lys	Ile	Trp 340	Asn											
	(2) INFO	RMAT	ION	FOR	SEQ	ID N	0:46	:								
30	(i)	(B) LE		: 41 amin	0 am	ino id	S: acid	s							
35	(ii)	MOL	ECUL	E TY	PE:	prot	ein									
	(iii)	HYP	OTHE	TICA	L: N	o				•						
40	(iv)	ANT	:I-SE	NSE :	МО											
	(vi)	ORI					OLATE	E: IE	F SS	:P 93	06,	Fig.	29			

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

- 117 -

	Met 1	Ala	Asp	Lys	Glu 5	Ala	Ala	Phe	Asp	Asp 10	Ala	Val	Glu	Glu	Arg 15	Va.
5	Ile	Asn	Glu	Glu 20	Tyr	Lys	Ile	Trp	Lys 25	Lys	Asn	Thr	Pro	Phe 30	Leu	Ty:
	Asp	Leu	Val 35	Met	Thr	His	Ala	Leu 40	Glu	Trp	Pro	Ser	Leu 45	Thr	Ala	Glı
10	Trp	Leu 50	Pro	Asp	Val	Thr	Arg 55	Pro	Glu	Gly	Lys	Asp 60	Phe	Ser	Ile	His
15	Arg 65	Leu	Val	Leu	Gly	Thr 70	His	Thr	Ser	Asp	Glu 75	Gln	Asn	His	Leu	Va] 80
	Ile	Ala	Ser	Val	Gln 85	Leu	Pro	Asn	Asp	Asp 90	Ala	Gln	Phe	Asp	Ala 95	Ser
20	His	Tyr	Asp	Ser 100	Glu	Lys	Gly	Glu	Phe 105	Gly	Gly	Phe	Gly	Ser 110	Val	Ser
	Gly	Lys	Ile 115	Glu	Ile	Glu	Ile	Lys. 120	Ile	Asn	His	Glu	Gly 125	Glu	Val	Asn
25	Arg	Ala 130		Tyr	Met	Pro	Gln 135	Asn	Pro	Cys	Ile	Ile 140	Ala	Thr	Lys	Thr
30	Pro 145	Ser	Ser	Asp	Val	Leu 150	Val	Phe	Asp	Tyr	Thr 155	Lys	His	Pro	Ser	Lys 160
	Pro	Asp	Pro	Ser	Gly 165	Glu	Cys	Asn	Pro	Asp 170	Leu	Arg	Leu	Arg	Gly 175	His
35	Gln	Lys	Glu	Gly 180	Tyr	Gly	Leu	Ser	Trp 185	Asn	Pro	Asn	Leu	Ser 190	Gly	His
	Leu	Leu	Ser 195	Ala	Ser	Asp	Asp	His 200	Thr	Ile	Cys	Leu	Trp 205	Asp	Ile	Ser
40	Ala	Val 210	Pro	Lys	Glu	Gly	Lys 215	Val	Val	Asp	Ala	Lys 220	Thr	Ile	Phe	Thr
45	Gly 225	His	Thr	Ala	Val	Val 230	Glu	Asp	Val	Ser	Trp 235	His	Leu	Leu	His	Glu 240
	Ser	Leu	Phe	Gly	Ser	Val	Ala	Asp	qzA	Gln	Lys	Leu	Met	Ile	Trp	Ast

- 118 -

. 250 Thr Arg Ser Asn Asn Thr Ser Lys Pro Ser His Ser Val Asp Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr Val Ala Leu Trp Asp Leu Arg Asn Leu Lys Leu Lys Leu His Ser Phe Glu Ser His Lys Asp Glu Ile Phe Gln Val Gln Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr Asp Arg Arg Leu Asn Val Trp Asp Leu Ser Lys Ile Gly Glu Glu Gln Ser Pro Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Val Trp Gln Met Glu Leu Val Leu Asp His (2) INFORMATION FOR SEQ ID NO:47: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 317 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- 119 -

(C) INDIVIDUAL ISOLATE: HUMAN 12.3, Fig. 30

	(xi)	SEQ	JENCI	E DES	CRI	PTIO	N: SI	EQ II	ON C	:47:						
5	Met 1	Thr	Glu	Gln	Met 5	Thr	Leu	Arg	Gly	Thr	Leu	Lys	Gly	His	Asn 15	Gl
10	Trp	Val	Thr	Gln 20	Ile	Ala	Thr	Thr	Pro 25	Gln	Phe	Pro	Asp	Met 30	Ile	Lei
	Ser	Ala	Ser 35	Arg	Asp	Lys	Thr	Ile 40	Ile	Met	Trp	Lys	Leu 45	Thr	Arg	Ası
15	Glu	Thr 50	Asn	Tyr	Gly	Ile	Pro 55	Gln	Arg	Ala	Leu	Arg 60	Gly	His	Ser	His
20	Phe 65	Val	Ser	Asp	Val	Val 70	Ile	Ser	Ser	Asp	Gly 75	Gln	Phe	Ala	Leu	Se:
	Gly	Ser	Trp	Asp	Gly 85	Thr	Leu	Arg	Leu	Trp 90	Asp	Leu	Thr	Thr	Gly 95	Thi
25	Thr	Thr	Arg	Arg 100	Phe	Val	Gly	His	Thr 105	Lys	Asp	Val	Leu	Ser 110	Val	Ala
	Phe	Ser	Ser 115	Asp	Asn	Arg	Gln	Ile 120	Val	Ser	Gly	Ser	Arg 125	Asp	Lys	Thi
30	Ile	Lys 130	Leu	Trp	Asn	Thr	Leu 135	Gly	Val	Cys	Lys	Tyr 140	Thr	Val	Gln	Ası
35	Glu 145	Ser	His	Ser	Glu	Trp 150	Val	Ser	Cys	Val	Arg 155	Phe	Ser	Pro	Asn	Ser 160
	Ser	Asn	Pro	Ile	Ile 165	Val	Ser	Cys	Gly	Trp 170	Asp	Lys	Leu	Val	Lys 175	Val
40	Trp	Asn	Leu	Ala 180	Asn	Cys	Lys	Leu	Lys 185	Thr	Asn	His	Ile	Gly 190	His	Thi
	Gly	Tyr	Leu 195	Asn	Thr	Val	Thr	Val 200	Ser	Pro	Asp	Gly	Ser 205	Leu	Cys	Ala
45	Ser	Gly 210	Gly	Lys	Asp	Gly	Gln 215	Ala	Met	Leu	Trp	Asp 220	Leu	Asn	Glu	Gl

- 120 -

	Lys :	His Leu	Tyr Thr I	eu Asp 30	Gly Gly	Asp Ile 235	Ile Asn	Ala Leu	Cys 240
5	Phe	Ser Pro	Asn Arg 7	yr Trp	Leu Cys	Ala Ala 250	Thr Gly	Pro Ser 255	Ile
	Lys	Ile Trp	Asp Leu 0	Slu Gly	Lys Ile 265	Ile Val	Asp Glu	Leu Lys 270	Gln
10	Glu	Val Ile 275	Ser Thr S	Ser Ser	Lys Ala 280	Glu Pro	Pro Gln 285	Cys Thr	Ser
15		Ala Trp 290	Ser Ala A	Asp Gly 295	Gln Thr	Leu Phe	Ala Gly 300	Tyr Thr	Asp
13	Asn 305	Leu Val	Arg Val 1	Trp Gln	Val Thr	Ile Gly 315	Thr Arg		
20	(2) INFOR		_						
	(1)	(A) LEN	E CHARACTE NGTH: 425 PE: amino POLOGY: ur	amino a					
25	(ii)		TYPE: p						
20			rical: No						÷.
30			L SOURCE:						
35		(C) INI	OIVIDUAL :	ISOLATE	: IEF -7	142 - hui	man, Fig	. 31	
	(xi)	SEQUENCI	E DESCRIP	rion: Si	EQ ID NO	:48:			•
40	Met 1	Ala Ser	Lys Glu i	Met Phe	Glu Asp	Thr Val	Glu Glu	Arg Val 15	Ile
••	Asn	Glu Glu	Tyr Lys :	Ile Trp	Lys Lys 25	Asn Thr	Pro Phe	Leu Tyr	Asp
45	Leu	Val Met	Thr His	Ala Leu	Gln Trp	Pro Ser	Leu Thr	Val Gln	Trp

- 121 -

	Leu	Pro 50	Glu	Val	Thr	Lys	Pro 55	Glu	Gly	Lys	Asp	Tyr 60	Ala	Leu	His	Trp
5	Leu 65	Val	Leu	Gly	Thr	His 70	Thr	Ser	Asp	Glu	Gln 75	Asn	His	Leu	Val	Val 80
	Ala	Arg	Val	His	Ile 85	Pro	Asn	Asp	Asp	Ala 90	Gln	Phe	Asp	Ala	Ser 95	His
10	Cys	Asp	Ser	Asp 100	Lys	Gly	Glu	Phe	Gly 105	Gly	Phe	Gly	Ser	Val 110	Thr	Gly
15	Lys	Ile	Glu 115	Cys	Glu	Ile	Lys	Ile 120	Asn	His	Glu	Gly	Glu 125	Val	Asn	Arg
15	Ala	Arg 130	Tyr	Met	Pro	Gln	Asn 135	Pro	His	Ile	Ile	Ala 140	Thr	Lys	Thr	Pro
20	Ser 145	Ser	Asp	Val	Leu	Val 150	Phe	Asp	Tyr	Thr	Lys 155	His	Pro	Ala	Lys	Pro 160
	Asp	Pro	Ser	Gly	Glu 165	Cys	Asn	Pro	Asp	Leu 170	Arg	Leu	Arg	Gly	His 175	Gln
25	Lys	Glu	_	Tyr 180	Gly	Leu	Ser	Trp	Asn 185	Ser	Asn	Leu	Ser	Gly 190	His	Leu
30	Leu	Ser	Ala 195	Ser	Asp	Asp	His	Thr 200	Val	Cys	Leu	Trp	Asp 205	Ile	Asn	Ala
	Gly	Pro 210	-	Glu	Gly	Lys	Ile 215		Asp	Ala	Lys	Ala 220	Ile	Phe	Thr	Gly
35	His 225	Ser	Ala	Val	Val	Glu 230	Asp	Val	Ala	Trp	His	Leu	Leu	His	Glu	Ser 240
	Leu	Phe	Gly	Ser	Val 245	Ala	Asp	Asp	Gln	Lys 250	Leu	Met	Ile	Trp	Asp 255	Thr
40	Arg	Ser	Asn	Thr 260		Ser	Lys	Pro	Ser 265		Leu	Val	Asp	Ala 270	His	Thr
45	Ala	Glu	Val 275		Суз	Leu	. Ser	Phe 280		Pro	Tyr	Ser	Glu 285	Phe	Ile	Leu
~~	Ala	Thr	Gly	Ser	Ala	Asp	Lys	Thr	Val	Ala	Leu	Trp	Asp	Leu	Arg	Asn

- 122 -

295 290 300 Leu Lys Leu Lys Leu His Thr Phe Glu Ser His Lys Asp Glu Ile Phe 305 310 315 320 5 Gln Val His Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly 325 330 335 Thr Asp Arg Arg Leu Asn Val Trp Asp Leu Ser Lys Ile Gly Glu Glu 10 340 345 350 Gln Ser Ala Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe Ile 355 360 365 15 His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn 370 375 380 Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Ile 385 390 395 20 Trp Gln Met Ala Glu Asn Ile Tyr Asn Asp Glu Glu Ser Asp Val Thr 405 410 Thr Ser Glu Leu Glu Gly Gln Gly Ser 25 420 425 (2) INFORMATION FOR SEQ ID NO:49: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 605 amino acids 30 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 40 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Insulin-like growth factor binding protein complex, Fig. 32

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Met Ala Leu Arg Lys Gly Gly Leu Ala Leu Ala Leu Leu Leu Leu Ser.

- 123 -

	1				5			•		10					15	
_	Trp	Val	Ala	Leu 20	Gly	Pro	Arg	Ser	Leu 25	Glu	Gly	Ala	Asp	Pro 30	Gly	Thr
5	Pro	Gly	Glu 35	Ala	Glu	Gly	Pro	Ala 40	Cys	Pro	Ala	Ala	Cys 45	Val	Cys	Ser
10	Tyr	Asp 50	Asp	Asp	Ala	Asp	Glu 55	Leu	Ser	Val	Phe	Суs 60	Ser	Ser	Arg	Asn
	Leu 65	Thr	Arg	Leu	Pro	Asp 70	Gly	Val	Pro	Gly	Gly 75	Thr	Gln	Ala	Leu	Trp 80
15	Leu	Asp	Gly	Asn	Asn 85	Leu	Ser	Ser	Val	Pro 90	Pro	Ala	Ala	Phe	Gln 95	Asn
20	Leu	Ser	Ser	Leu 100	Gly	Phe	Leu	Asn	Leu 105	Gln	Gly	Gly	Gln	Leu 110	Gly	Ser
	Leu	Glu	Pro 115		Ala	Leu	Leu	Gly 120	Leu	Glu	Asn	Leu	Cys 125	His	Leu	His
25	Leu	Glu 130	Arg	Asn	Gln	Leu	Arg 135	Ser	Leu	Ala	Leu	Gly 140	Thr	Phe	Ala	His
	Thr 145	Pro	Ala	Leu	Ala	Ser	Leu	Gly	Leu	Ser	Asn 155		Arg	Leu	Ser	Arg 160
30	Leu	Glu	Asp	Gly	Leu 165	Phe	Glu	Gly	Leu	Gly 170	Ser	Leu	Trp	Asp	Leu 175	Asn
35	Leu	Gly	Trp	Asn 180	Ser	Leu	Ala	Val	Leu 185	Pro	Asp	Ala	Ala	Phe 190	Arg	Gly
	Leu	Gly	Ser 195	Leu	Arg	Glu	Leu	Val 200	Leu	Ala	Gly	Asn	A rg 205	Leu	Ala	Tyr
40	Leu	Gln 210		Ala	Leu	Phe	Ser 215	Gly	Leu	Ala	Glu	Leu 220	Arg	Glu	Leu	Asp
·	Leu 225		Arg	Asn	Ala	Leu 230		Ala	Ile	Lys	Ala 235	Asn	Val	Phe	Val	Gln 240
45	Leu	Pro	Arg	Leu	Gln 245	_	Leu	Tyr	Leu	Asp 250		Asn	Leu	Ile	Ala 255	Ala

- 124 -

	Val	Ala	Pro	Gly 260	Ala	Phe	Leu	Gly	Leu 265	Lys	Ala	Leu	Arg	Trp 270	Leu	Asp
5	Leu	Ser	His 275	Asn	Arg	Val	Ala	Gly 280	Leu	Leu	Glu	Asp	Thr 285	Phe	Pro	Gly
·	Leu	Leu 290	Gly	Leu	Arg	Val	Leu 295	Arg	Leu	Ser	His	Asn 300	Ala	Ile	Ala	Ser
10	Leu 305	Arg	Pro	Arg	Thr	Phe 310	Lys	Asp	Leu	His	Phe 315	Leu	Glu	Glu	Leu	Gln 320
15	Leu	Gly	His	Asn	Arg 325	Ile	Arg	Gln	Leu	Ala 330	Glu	Arģ	Ser	Phe	Glu 335	Gly
	Leu	Gly	Gln	Leu 340	Glu	Val	Leu	Thr	Leu 345	Asp	His	Asn	Gln	Leu 350	Gln	Glu
20	Val	Lys	Ala 355	Gly	Ala	Phe	Leu	Gly 360	Leu	Thr	Asn	Val	Ala 365	Val	Met	Asn
	Leu	Ser 370	Gly	Asn	Cys	Leu	Arg 375	Asn	Leu	Pro	Glu	Gln 380	Val	Phe	Arg	Gly
25	Leu 385	Gly	Lys	Leu	His	Ser 390	Leu	His	Leu	Glu	Gly 395	Ser	Cys	Leu	Gly	Arg 400
30	Ile	Arg	Pro	His	Thr 405	Phe	Thr	Gly	Leu	Ser 410	Gly	Leu	Arg	Arg	Leu 415	Phe
	Leu	Lys	Asp	Asn 420	Gly	Leu	Val	Gly	Ile 425	Glu	Glu	Gln	Ser	Leu 430	Trp	Gly
35			Glu 435					440					445			
		450					455	-		-	-	460		-		
40	465		Arg		_	470					475					480
45			Arg Asn		485	-		-		490			_		495	
										1	3		3	- 3 -		

- 125 -

505 510 500 Leu Arg Asn Asn Ser Leu Arg Thr Phe Thr Pro Gln Pro Pro Gly Leu 520 525 515 5 Glu Arg Leu Trp Leu Glu Gly Asn Pro Trp Asp Cys Gly Cys Pro Leu 535 .530 Lys Ala Leu Arg Asp Phe Ala Leu Gln Asn Pro Ser Ala Val Pro Arg 545 550 555 560 10 Phe Val Gln Ala Ile Cys Glu Gly Asp Asp Cys Gln Pro Pro Ala Tyr 565 570 575 Thr Tyr Asn Asn Ile Thr Cys Ala Ser Pro Pro Glu Val Val Gly Leu 15 585 590 580 Asp Leu Arg Asp Leu Ser Glu Ala His Phe Ala Pro Cys 595 600 605 20 (2) INFORMATION FOR SEQ ID NO:50: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 603 amino acids (B) TYPE: amino acid 25 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 35 (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind. pro. complex-rat, Fig. 33 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50: Met Ala Leu Arg Thr Gly Gly Pro Ala Leu Val Val Leu Leu Ala Phe 40 5 10 Trp Val Ala Leu Gly Pro Cys His Leu Gln Gly Thr Asp Pro Gly Ala 20 25 30 45

Ser Ala Asp Ala Glu Gly Pro Gln Cys Pro Val Ala Cys Thr Cys Ser

- 126 -

		•	35					40					45			
5	His	Asp 50	Asp	Tyr	Thr	Asp	Glu 55	Leu	Ser	Val	Phe	Cys 60	Ser	Ser	Lys	Asn
	Leu 65	Thr	His	Leu	Pro	Asp 70	Asp	Ile	Pro	Val	Ser 75	Thr	Arg	Ala	Leu	Trp 80
10	Leu	Asp	Gly	Asn	Asn 85	Leu	Ser	Ser	Ile	Pro 90	Ser	Ala	Ala	Phe	Gln 95	Asn
	Leu	Ser	Ser	Leu 100	Asp	Phe	Leu	Asn	Leu 105	Gln	Gly	Ser	Trp	Leu 110	Arg	Ser
15	Leu	Glu	Pro 115	Gln	Ala'	Leu	Leu	Gly 120	Leu	Gln	Asn	Leu	Tyr 125	Tyr	Leu	His
20	Leu	Glu 130	Arg	Asn	Arg	Leu	Arg 135	Asn	Leu	Ala	Val	Gly 140	Leu	Phe	Thr	His
20	Thr 145	Pro	Ser	Leu	Ala	Ser 150	Leu	Ser	Leu	Ser	Ser 155	Asn	Leu	Leu	Gly	Arg 160
25	Leu	Glu	Glu	Gly	Leu 165	Phe	Gln	Gly	Leu	Ser 170	His	Leu	Trp	Asp	Leu 175	Asn
	Leu	Gly	Trp	Asn 180	Ser	Leu	Val	Val	Leu 185	Pro	Asp	Thr	Val	Phe 190	Gln	Gly
30	Leu	Gly	Asn 195	Leu	His	Glu	Leu	Val 200	Leu	Ala	Gly	Asn	Lys 205	Leu	Thr	Tyr
35	Leu	Gln 210	Pro	Ala	Leu	Phe	Cys 215	Gly	Leu	Gly	Glu	Leu 220	Arg	Glu	Leu	Asp
	Leu 225	Ser	Arg	Asn	Ala	Leu 230	Arg	Ser	Val	Lys	Ala 235	Asn	Val	Phe	Val	His 240
40	Leu	Pro	Arg	Leu	Gln 245	Lys	Leu	Tyr	Leu	Asp 250	Arg	Asn	Leu	Ile	Thr 255	Ala
	Val	Ala	Pro	Gly 260	Ala	Phe	Leu	Gly	Met 265	Lys	Ala	Leu	Arg	Trp 270	Leu	Asp
45	Leu	Ser	His	Asn	Arg	Val		Gly	Leu	Met	Glu	Asp	Thr	Phe	Pro	Gly

- 127 -

	Leu	Leu 290	Gly	Leu	His	Val	Leu 295	Arg	Leu	Ala	His	Asn 300	Ala	Ile	Ala	Ser
5	Leu 305	Arg	Pro	Arg	Thr	Phe 310	Lys	Asp	Leu	His	Phe 315	Leu	Glu	Glu	Leu	Gln 320
	Leu	Gly	His	Asn	Arg 325	Ile	Arg	Gln	Leu	Gly 330	Glu	Arg	Thr	Phe	Glu 335	Gly
10	Leu	Gly	Gln	Leu 340	Glu	Val	Leu	Thr	Leu 345	Asn	Asp	Asn	Gln	Ile 350	Thr	Glu
15	Val	Arg	Val 355	Gly	Ala	Phe	Ser	Gly 360	Leu	Phe	Asn	Val	Ala 365	Val	Met	Asn
	Leu	Ser 370	Gly	Asn	Cys	Leu	Arg 375	Ser	Leu	Pro	Glu	Arg 380	Val	Phe	Gln	Gly
20	Leu 385	Asp	Lys	Leu	His	Ser 390	Leu	His	Leu	Glu	His 395	Ser	Cys	Leu	Gly	His 400
	Val	Arg	Leu	His	Thr 405	Phe	Ala	Gly	Leu	Ser 410	Gly	Leu	Arg	Arg	Leu 415	Phe
25	Leu	Arg	Asp	Asn 420	Ser	Ile	Ser	Ser	Ile 425	Glu	Glu	Gln	Ser	Leu 430	Ala	Gly
30	Leu	Ser	Glu 435	Leu	Leu	Glu	Leu	Asp 440	Leu	Thr	Thr	Asn	Arg 445	Leu	Thr	His
	Leu	Pro 450	Arg	Gln	Leu	Phe	Gln 455	Gly	Leu	Gly	His	Leu 460	Glu	Tyr	Leu	Leu
35	Leu 465	Ser	Tyr	Asn	Gln	Leu 470	Thr	Thr	Leu	Ser	Ala 475	Glu	Val	Leu	Gly	Pro 480
	Leu	Gln	Arg	Ala	Phe 485	Trp	Leu	Asp	Ile	Ser 490	His	Asn	His	Leu	Glu 495	Thr
40	Leu	Ala	Glu	Gly 500	Leu	Phe	Ser	Ser	Leu 505	Gly	Arg	Val	Arg	Tyr 510	Leu	Ser
4 5	Leu	Arg	Asn 515	Asn	Ser	Ĺeu	Gln	Thr 520	Phe	Ser	Pro	Gln	Pro 525	Gly	Leu	Glu
	Arg	Leu	Trp	Leu	Asp	Ala	Asn	Pro	Trp	Asp	Cys	Ser	Cys	Pro	Leu	Lys

- 128 -Ala Leu Arg Asp Phe Ala Leu Gln Asn Pro Gly Val Val Pro Arg Phe Val Gln Thr Val Cys Glu Gly Asp Asp Cys Gln Pro Val Tyr Thr Tyr Asn Asn Ile Thr Cys Ala Gly Pro Ala Asn Val Ser Gly Leu Asp Leu Arg Asp Val Ser Glu Thr His Phe Val His Cys (2) INFORMATION FOR SEQ ID NO:51: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 409 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: LIS1 (human), Fig. 34 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51: Met Val Leu Ser Gln Arg Gln Arg Asp Glu Leu Asn Arg Ala Ile Ala Asp Tyr Leu Arg Ser Asn Gly Tyr Glu Glu Ala Tyr Ser Val Phe Lys Lys Glu Ala Glu Leu Asp Val Asn Glu Glu Leu Asp Lys Lys Tyr Ala

Val Met Glu Leu Glu Ser Lys Leu Asn Glu Ala Lys Glu Glu Phe Thr

Gly Leu Leu Glu Lys Lys Trp Thr Ser Val Ile Arg Leu Gln Lys Lys

- 129 -

	65					70					75					80
-	Ser	Gly	Gly	Pro	Leu 85	Gly	Gln	Lys	Arg	Asp 90	Pro	Lys	Glu	Trp	Ile 95	Pro
5	Arg	Pro	Pro	Glu 100	Lys	Tyr	Ala	Leu	Ser 105	Gly	His	Arg	Ser	Pro 110	Val	Thr
10	Arg	Val	Ile 115	Phe	His	Pro	Val	Phe 120	Ser	Val	Met	Val	Ser 125	Ala	Ser	Glu
	Asp	Ala 130	Thr	Ile	Lys	Val	Trp 135	Asp	Tyr	Glu	Thr	Gly 140	Asp	Phe	Glu	Arg
15	Thr 145	Leu	Lys	Gly	His	Thr 150	Asp	Ser	Val	Gln	Asp 155	Ile	Ser	Phe	Asp	His
20	Ser	Gly	Lys	Leu	Leu 165	Ala	Ser	Cys	Ser	Ala 170	Asp	Met	Thr	Ile	Lys 175	Leu
	Trp	Asp	Phe	Gln 180	Gly	Phe	Glu	Cys	Ile 185	Arg	Thr	Met	His	Gly 190	His	Asp
25	His	Asn	Val 195	Ser	Ser	Val	Ala	Ile 200	Met	Pro	Asn	Gly	Asp 205	His	Ile	Val
	Ser	Ala 210	Ser	Arg	Asp	Lys	Thr 215	Ile	Lys	Met	Trp	Glu 220	Val	Gln	Thr	Gly
30	Tyr 225	Cys	Val	Lys	Thr	Phe 230	Thr	Gly	His	Arg	Glu 235	Trp	Val	Arg	Met	Val 240
35	Arg	Pro	Asn	Gln	Asp 245	Gly	Thr	Leu	Ile	Ala 250	Ser	Cys	Ser	Asn	Asp 255	Glr
	Thr	Val	Arg	Val 260	Trp	Val	Val	Ala	Thr 265	Lys	Glu	Cys	Lys	Ala 270	Glu	Lev
40	Arg	Glu	His 275	Glu	His	Val	Val	Glu 280	Сув	Ile	Ser	Trp	Ala 285	Pro	Glu	Ser
	Ser	Tyr 290		Ser	Ile	Ser	Glu 295	Ala	Thr	Gly	Ser	Glu 300	Thr	Lys	Lys	Sei
45	Gly 305	_	Pro	Gly	Pro	Phe		Leu	Ser	Gly	Ser	_	Asp	Lys	Thr	Ly:

- 130 -

	Met Trp Asp Val Ser Thr Gly Met Cys Leu Met Thr Leu Val Gly His 325 330 335	
5	Asp Asn Trp Val Arg Gly Val Leu Phe His Ser Gly Gly Lys Phe Ile 340 345 350	
	Leu Ser Cys Ala Asp Asp Lys Thr Leu Arg Val Trp Asp Tyr Lys Asn 355 360 365	
10	Lys Arg Cys Met Lys Thr Leu Asn Ala His Glu His Phe Val Thr Ser 370 375 380	
15	Leu Asp Phe His Lys Thr Ala Pro Tyr Val Val Thr Gly Ser Val Asp 385 390 395 400	
13	Gln Thr Val Lys Val Trp Glu Cys Arg 405	
20	(2) INFORMATION FOR SEQ ID NO:52:	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 422 amino acids (B) TYPE: amino acid	
	(D) TOPOLOGY: unknown	
25	(ii) MOLECULE TYPE: protein	
	(iii) HYPOTHETICAL: NO	
30	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MD6, Fig. 35	
35	·	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:	
40	Met Glu Arg Lys Asp Phe Glu Thr Trp Leu Asp Asn Ile Ser Val Thr 1 5 10 15	
	Phe Leu Ser Leu Met Asp Leu Gln Lys Asn Glu Thr Leu Asp His Leu 20 25 30	
45	Ile Ser Leu Ser Gly Ala Val Gln Leu Arg His Leu Ser Asn Asn Leu 35 40 45	

- 131 -

	GIu	Thr 50	Ļeu	Leu	Lys	Arg	Asp 55	Phe	Leu	Lys	Leu	Leu 60	Pro	Leu	Glu	Leu
5	Ser 65	Phe	Tyr	Leu	Leu	Lys 70	Trp	Leu	Asp	Pro	Gln 75	Thr	Leu	Leu	Thr	Cys 80
•	Cys	Leu	Val	Ser	Lys 85	Gln	Arg	Asn	Lys	Val 90	Ile	Ser	Ala	Cys	Thr 95	Glu
10	Val	Trp	Gln	Thr 100	Ala	Cys	Lys	Asn	Leu 105	Gly	Trp	Gln	Ile	Asp 110	Asp	Ser
15	Val	Gln	Asp 115	Ser	Leu	His	Trp	Lys 120	Lys	Val	Tyr	Leu	Lys 125	Ala	Ile	Leu
	Arg	Met 130	Lys	Gln	Leu	Glu	Asp 135	His	Glu	Ala	Phe	Glu 140	Thr	Ser	Ser	Leu
20	Ile 145	Gly	His	Ser	Ala	Arg 150	Val	Tyr	Ala	Leu	Tyr 155	Tyr	Lys	Asp	Gly	Leu 160
	Leu	Cys	Thr	Gly	Ser 165	Asp	Asp	Leu	Ser	Ala 170	Lys	Leu	Trp	Asp	Val 175	Ser
25	Thr	Gly	Gln	Cys 180	Val	Tyr	Gly	Ile	Gln 185	Thr	His	Thr	Cys	Ala 190	Ala	Val
30	Lys	Phe	Asp 195	Glu	Gln	Lys	Leu	Val 200	Thr	Gly	Ser	Phe	Asp 205	Asn	Thr	Val.
	Ala	Cys 210	Trp	Glu	Trp	Ser	Ser 215	Gly	Ala	Arg	Thr	Gln 220	His	Phe	Arg	Gly
35	His 225	Thr	Gly	Ala	Val	Phe 230	Ser	Val	Asp	Týr	Ser 235	Asp	Glu	Leu	Asp	Ile 240
	Leu	Val	Ser	Gly	Ser 245	Ala	Asp	Phe	Ala	Val 250	Lys	Val	Trp	Ala	Leu 255	Ser
40	Ala	Gly	Thr	Cys 260	Leu	Asn	Thr	Leu	Thr 265	Gly	His	Thr	Glu	Trp 270	Val	Thr
45	Lys	Val	Val 275	Leu	Gln	Lys	Cys	Lys 280	Val	Lys	Ser	Leu	Leu 285	His	Ser	Pro
	Gly	Asp	Tyr	Ile	Leu	Leu	Ser	Ala	Asp	Lys	Tyr	Glu	Ile	Lys	Ile	Trp

- 132 -

295 290 300 Pro Ile Gly Arg Glu Ile Asn Cys Lys Cys Leu Lys Thr Leu Ser Val 305 310 315 320 5 Ser Glu Asp Arg Ser Ile Cys Leu Gln Pro Arg Leu His Phe Asp Gly 330 325 335 Lys Tyr Ile Val Cys Ser Ser Ala Leu Gly Leu Tyr Gln Trp Asp Phe 10 340 345 350 Ala Ser Tyr Asp Ile Leu Arg Val Ile Lys Thr Pro Glu Val Ala Asn 355 360 365 15 Leu Ala Leu Leu Gly Phe Gly Asp Val Phe Ala Leu Leu Phe Asp Asn 370 375 His Tyr Leu Tyr Ile Met Asp Leu Arg Thr Glu Ser Leu Ile Ser Arg 385 390 395 20 Trp Pro Leu Pro Glu Tyr Arg Lys Ser Lys Arg Gly Thr Ser Phe Leu 405 410 Ala Gly Glu Arg Pro Gly 25 420 (2) INFORMATION FOR SEQ ID NO:53: (i) SEQUENCE CHARACTERISTICS: 30 (A) LENGTH: 422 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 40 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MSL1, Fig. 36

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

45

Met Asn Gln Cys Ala Lys Asp Ile Thr His Glu Ala Ser Ser Ile Pro

- 133 -

	1				5					10					15	
5	Ile	Asp	Leu	Gln 20	Glu	Arg	Tyr	Ser	His 25	Trp	Lys	Lys	Asn	Thr 30	Lys	Leu
	Leu	Tyr	Asp 35	Tyr	Leu	Asn	Thr	Asn 40	Ser	Thr	Lys	Trp	Pro 45	Ser	Leu	Thr
10	Cys	Gln 50	Phe	Phe	Pro	Asp	Leu 55	Asp	Thr	Thr	Ser	Asp 60	Glu	His	Arg	Ile
	Leu 65	Leu	Ser	Ser	Phe	Thr 70	Ser	Ser	Gln	Lys	Pro 75	Glu	Asp	Glu	Thr	Ile 80
15	Tyr	Ile	Ser	Lys	Ile 85	Ser	Thr	Leu	Gly	His 90	Ile	Lys	Trp	Ser	Ser 95	Leu
20	Asn	Asn	Phe	Asp 100	Met	Asp	Glu	Met	Glu 105	Phe	Lys	Pro	Glu	Asn 110	Ser	Thr
	Arg	Phe	Pro 115		Lys	His	Leu	Val 120	Asn	Asp	Ile	Ser	Ile 125	Phe	Phe	Pro
25	Asn	Gly 130	Glu	Cys	Asn	Arg	Ala 135	Arg	Tyr	Leu	Pro	Gln 140	Asn	Pro	Asp	Ile
	Ile 145	Ala	Gly	Ala	Ser	Ser	Asp	Gly	Ala	Ile	Tyr 155	Ile	Phe	Asp	Arg	Thr 160
30	Lys	His	Gly	Ser	Thr 165	Arg	Ile	Arg	Gln	Ser 170	Lys	Ile	Ser	His	Pro 175	Phe
35	Glu	Thr	Lys	Leu 180	Phe	Gly	Ser	His	Gly 185	Val	Ile	Gln	Asp	Val 190	Glu	Ala
	Met	Asp	Thr 195	Ser	Ser	Ala	Asp	Ile 200	Asn	Glu	Ala	Thr	Ser 205	Leu	Ala	Trp
40	Asn	Leu 210	Gln	Gln	Glu	Ala	Leu 215	Leu	Leu	Ser	Ser	His 220	Ser	Asn	Gly	Gln
	Val 225	Gln	Val	Trp	Asp	Ile 230	Lys	Gln	Tyr	Ser	His 235	Glu	Asn	Pro	Ile	Ile 240
45	Asp	Leu	Pro	Leu	Val 245	Ser	Ile	Asn	Ser	Asp 250	Gly	Thr	Ala	Val	Asn 255	Asp

- 134 -

	Val	Thr	Trp	Met 260	Pro	Thr	His	Asp	Ser 265	Leu	Phe	Ala	Ala	Cys 270	Thr	Glu
5	Gly	Asn	Ala 275	Val	Ser	Leu	Leu	Asp 280	Leu	Arg	Thr	Lys	Lys 285	Glu	Lys	Leu
•	Gln	Ser 290	Asn	Arg	Glu	Lys	His 295	Asp	Gly	Gly	Val	Asn 300	Ser	Cys	Arg	Phe
10	Asn 305	Tyr	Lys	Asn	Ser	Leu 310	Ile	Leu	Ala	Ser	Ala 315	Asp	Ser	Asn	Gly	Arg 320
15	Leu	Asn	Leu	Trp	Asp 325	Ile	Arg	Asn	Met	Asn 330	Lys	Ser	Pro	Ile	Ala 335	Thr
	Met	Glu	His	Gly 340	Thr	Ser	Val	Ser	Thr 345	Leu	Glu	Trp	Ser	Pro 350	Asn	Phe
20	Asp	Thr	Val 355	Leu	Ala	Thr	Ala	Gly 360	Gln	Glu	Asp	Gly	Leu 365	Val	Lys	Leu
	Trp	Asp 370	Thr	Ser	Cys	Glu	Glu 373	Thr	Ile	Phe	Thr	His 380	Gly	Gly	His	Met
25	Leu 385	Gly	Val	Asn	Asp	Ile 390	Ser	Trp	Asp	Ala	His 395	Asp	Pro	Trp	Leu	Met 400
30	Cys	Ser	Val	Ala	Asn 405	Asp	Asn	Ser	Val	His 410	Ile	Trp	Lys	Pro	Ala 415	Gly
				Gly 420							•					
35	(2) INFO	RMAT:	ION 1	FOR S	SEQ :	ID NO	0:54	:								
	(i)	(A)) LEI	NGTH PE: 4	: 810 amin	reris 6 am: o ac: unkno	ino a		5							
40	(ii)	MOL	ECUL	E TY	PE:]	prot	ein									
	(iii)	HYP	OTHE	TICA	L: N	0										

45 (iv) ANTI-SENSE: NO

- 135 -

	(vi)		IANIE INI				LATE	: MU	S MU	SCULI	US PI	ROTE	IN,	Fig.	37	
5	(xi)	SEQ	JENCI	E DES	SCRII	PTIO	N: S1	EQ II	on c	:54:				٠		
	Phe 1	Arg	Met	Asp	Asn 5	Ala	Ser	Thr	Arg	Ile 10	Asp	Glu	Arg	Phe	Arg 15	Ile
10	Asp	Ala	Tyr	Ala 20	Asn	Ála	Arg	Tyr	Pro 25	Met	Pro	Arg	Thr	Glu 30	Ile	Asn
15	Ser	Glu	Gln 35	Glu	Asn	Cys	Glu	Asn 40	Thr	Ile	Thr	Leu	Glu 45	Asp	Ser	Glu
	Gln	Glu 50	Asn	Cys	Glu	Ala	Ala 55	Cys	Met	Pro	Leu	Glu 60	Thr	Glu	Ser	Glu
20	Gln 65	Glu	Asn	Cys	Glu	Met 70	Ser	Ser	His	Glu	Ser 75	Tyr	Thr	Asn	Ala	Ala 80
	Glu	Thr	Pro	Glu	Asn 85	Ile	Ser	Ile	Leu	Ser 90	Cys	Leu	Gly	Glu	Thr 95	Ser
25	Gly	Ala	Leu	Val 100	Asp	Thr	Lys	Thr	Ile 105	Ser	Asp	Ile	Lys	Thr 110	Met	Asp
30	Pro	Arg	Val	Ser	Leu	Thr	Pro	Ser 120	Ser	Asp	Val	Thr	Gly 125	Thr	Glu	Asp
	Ser	Ser 130	Val	Leu	Thr	Pro	Gln 135	Ser	Thr	Asp	Val	Asn 140	Ser	Val	Asp	Ser
35	Tyr 145	Gln	Gly	Tyr	Glu	Gly 150	Asp	Asp	Asp	Asp	Glu 155	Glu	Asp	Asp	Glu	Asp 160
	Asp	Lys	Asp	Gly	Asp 165	Ser	Asn	Leu	Pro	Ser 170	Leu	Glu	Asp	Ser	Asp 175	Asn
10	Phe	Ile	Ser	Cys 180	Leu	Glu	Asn	Ser	Tyr 185	Ile	Pro	Gln	Asn	Val 190	Glu	Asn
15	Gly	Glu	Val 195	Val	Glu	Glu	Gln	Ser 200	Leu	Gly	Arg	Arg	Phe 205	His	Pro	Tyr
- -	Glu	Leu	Glu	Ala	Gly	Glu	Val	Val	Glu	Gly	Gln	Gly	Gly	Gly	Ser	Leu

- 136 -

Phe Tyr Pro Tyr Glu Leu Glu Ala Gly Glu Val Val Glu Ala Gln Asn Val Gln Asn Leu Phe His Arg Tyr Glu Leu Glu Glu Gly Glu Val Val Glu Ala Gln Val Val Gln Ser Met Phe Pro Tyr Tyr Glu Leu Glu'Ala Gly Glu Val Val Glu Ala Glu Glu Val Gln Gly Phe Phe Gln Arg Tyr Glu Leu Glu Ala Arq Glu Val Ile Gly Ala Gln Gly Gly Gln Gly Leu Ser Arg His Tyr Gly Leu Glu Gly Gly Glu Val Val Glu Ala Thr Ala Val Arg Arg Leu Ile Gln His His Glu Leu Glu Glu Gly Glu Asp Val Asp Asp Gln Glu Glu Ser Ser Glu Met His Glu Glu Thr Ser Glu Asp Ser Ser Glu Gln Tyr Asp Ile Glu Asp Asp Ser Leu Ile Asp Glu Trp Ile Ala Leu Glu Thr Ser Pro Leu Pro Arg Pro Arg Trp Asn Val Leu Ser Ala Leu Arg Asp Arg Gln Leu Gly Ser Ser Gly Arg Phe Val Tyr Glu Ala Cys Gly Ala Arg Leu Phe Val Gln Arg Phe Ser Leu Glu His Val Phe Glu Gly His Ser Gly Cys Val Asn Thr Val His Phe Asn Gln His Gly Thr Leu Leu Ala Ser Gly Ser Asp Asp Leu Lys Val Ile Val Trp Asp Trp Leu Lys Lys Arg Ser Val Leu Asn Phe Asp Ser Gly His

- 137 -

	Lys 465	Asn	Asn	Ile	Leu	Gln 470	Ala	Lys	Phe	Leu	Pro 475	Asn	Cys	Asn	Asp	Ala 480
5	Ile	Leu	Ala	Met	Cys 485	Gly	Arg	Asp	Gly	Gln 490	Val	Arg	Val	Ala	Gln 495	Leu
	Ser	Ala	Val	Ala 500	Gly	Thr	His	Met	Thr 505	Lys	Arg	Leu	Val	Lys 510	His	Gly
10	Gly	Ala	Ser 515	His	Arg	Leu	Gly	Leu 520	Glu	Pro	Asp	Ser	Pro 525	Phe	Arg	Phe
15	Leu	Thr 530	Ser	Gly	Glu	Asp	Ala 535	Val	Val	Phe	Asn	Ile 540	Asp	Leu	Arg	Gln
	Ala 545	His	Pro	Ala	Ser	Lys 550	Leu	Leu	Val	Ile	Lys 5 55	Asp	Gly	Asp	Lys	Lys 560
20	Val	Gly	Leu	Tyr	Thr 565	Val	Phe	Val	Asn	Pro 570	Ala	Asn	Val	Tyr	Gln 575	Phe
	Ala	Val	Gly	Gly 580	Gln	Asp	Gln	Phe	Met 585	Arg	Ile	Tyr	Asp	Gln 590	Arg	Lys
25	Ile	Asp	Glu 595	Asn	Val	Asn	Asn	Gly 600	Val	Leu	Lys	Lys	Phe 605	Cys	Pro	His
30	His	Leu 610	Leu	Ser	Ser	Asp	Tyr 615	Pro	Ala	His	Ile	Thr 620	Ser	Leu	Met	Tyr
•	625	•	•	•		630	Ile				635		-		-	640
35					645		Asp		_	650	,				655	
	•	•	-	660	_		Asn		665		-	-	•	670		
40			675				Val	680					685			
45		690	_				695	_				700				Ala
	Asp	Glu	Gly	Gly	Thr	Ile	: Asn	Cys	Ile	Asp	Ser	His	Pro	Tyr	Leu	Pro

- 138 -

710 715 705 Val Leu Ala Ser Ser Gly Leu Asp His Glu Val Lys Ile Trp Ser Pro 730 725 5 Ile Ala Glu Pro Ser Lys Lys Leu Ala Gly Leu Lys Asn Val Ile Lys 740 745 Ile Asn Lys Leu Lys Arg Asp Asn Phe Thr Leu Arg His Thr Ser Leu 760 755 10 Phe Asn Asn Ser Met Leu Cys Phe Leu Met Ser His Val Thr Gln Ser 770 775 Asn Tyr Gly Arg Ser Trp Arg Gly Ile Arg Ile Asn Ala Gly Gly 15 785 790 795 Asp Phe Ser Asp Ser Ser Ser Ser Glu Glu Thr Asn Gln Glu Ser 805 810 815 20 (2) INFORMATION FOR SEQ ID NO:55: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 422 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 35 (C) INDIVIDUAL ISOLATE: ORF RB1, Fig. 38 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: 40 Met Asn Gln Cys Ala Lys Asp Ile Thr His Glu Ala Ser Ser Ile Pro 5 1 10 Ile Asp Leu Gln Glu Arg Tyr Ser His Trp Lys Lys Asn Thr Lys Leu 20 25 45

- 139 -

	Leu	Tyr	Asp 35	Tyr	Leu	Asn	Thr	Asn 40	Ser	Thr	Lys	Trp	Pro 45	Ser	Leu	Th:
5	Cys	Gln 50	Phe	Phe	Pro	Asp	Leu 55	Asp	Thr	Thr	Ser	Asp 60	Glu	His	Arg	Ile
	Leu 65	Leu	Ser	Ser	Phe	Thr 70	Ser	Ser	Gln	Lys	Pro 75	Glu	Asp	Glu	Thr	Ile 80
10	Tyr	Įle	Ser	Lys	Ile 85	Ser	Thr	Leu	Gly	His 90	Ile	Lys	Trp	Ser	Ser 95	Let
15	Asn	Asn	Phe	Asp 100	Met	Asp	Glu	Met	Glu 105	Phe	Lys	Pro	Glu	Asn 110	Ser	Thi
	Arg	Phe	Pro 115	Ser	Lys	His	Leu	Val 120	Asn	Asp	Ile	Ser	Ile 125	Phe	Phe	Pro
20	Asn	Gly 130	Glu	Cys	Asn	Arg	Ala 135	Arg	Tyr	Leu	Pro	Gln 140	Asn	Pro	Asp	Ile
	Ile 145	Ala	Gly	Ala	Ser	Ser 150	Asp	Gly	Ala	Ile	Tyr 155	Ile	Phe	Asp	Arg	Thr
25	Lys	His	Gly	Ser	Thr 165	Arg	Ile	Arg	Gln	Ser 170	Lys	Ile	Ser	His	Pro 175	Phe
30	Glu	Thr	Lys	Leu 180	Phe	Gly	Ser	His	Gly 185	Val	Ile	Gln	Asp	Val 190	Glu	Ala
	Met	Asp	Thr 195	Ser	Ser	Ala	Asp	Ile 200	Asn	Glu	Ala	Thr	Ser 205	Leu	Ala	Trp
35	Asn	Leu 210	Gln	Gln	Glu	Ala	Leu 215	Leu	Leu	Ser	Ser	His 220	Ser	Asn	Gly	Gln
	Val 225	Gln	Val	Trp	Asp	Ile 230	Lys	Gln	Tyr	Ser	His 235	Glu	Asn	Pro	Ile	Ile 240
40	qaA	Leu	Pro	Leu	Val 245	Ser	Ile	Asn	Ser	Asp 250	Gly	Thr	Ala	Val	Asn 255	Asp
45	Val	Thr	Trp	Met 260	Pro	Thr	His	Asp	Ser 265	Leu	Phe	Ala	Ala	Cys 270	Thr	Glu
	Gly	Asn	Ala	Val	Ser	Leu	Leu	Asp	Leu	Arg	Thr	Lys	Lys	Glu	Lys	Let

- 140 -

275 280 285 Gln Ser Asn Arg Glu Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe 290 295 Asn Tyr Lys Asn Ser Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg 305 310 320 Leu Asn Leu Trp Asp Ile Arg Asn Met Asn Lys Ser Pro Ile Ala Thr 10 325 335 Met Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe 340 345 15 Asp Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu 355 360 Trp Asp Thr Ser Cys Glu Glu Thr Ile Phe Thr His Gly Gly His Met 370 375 380 20 Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro Trp Leu Met 385 390 400 Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys Pro Ala Gly 25 405 415 Asn Leu Val Gly His Ser 420 30 (2) INFORMATION FOR SEQ ID NO:56: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 576 amino acids (B) TYPE: amino acid 35 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 40 (iv) ANTI-SENSE: NO

(C) INDIVIDUAL ISOLATE: Periodic Trp protein, Fig. 39

(vi) ORIGINAL SOURCE:

- 141 -

	(xi)	SEQU	JENCE	DES	CRIE	MOIT	1: SE	EQ II	NO:	:56:						
5	Met 1	Ile	Ser	Ala	Thr 5	Asn	Trp	Val	Pro	Arg 10	Gly	Phe	Ser	Ser	Glu 15	Phe
J	Pro	Glu	Lys	Tyr 20	Val	Leu	Asp	Asp	Glu 25	Glu	Val	Glu	Arg	Ile 30	Asn	Gln
10	Leu	Ala	Gln 35	Leu	Asn	Leu	Asp	Asp 40	Ala	Lys	Ala	Thr	Leu 45	Glu	Glu	Ala
	Glu	Gly 50	Glu	Ser	Gly	Val	Glu 55	Asp	Asp	Ala	Ala	Thr 60	Gly	Ser	Ser	Asn
15	Lys 65	Leu	Lys	Asp	Gln	Leu 70	Asp	Ile	Asp	Asp	Asp 75	Leu	Lys	Glu	Tyr	Asn 80
20	Leu	Glu	Glu	Tyr	Asp 85	Asp	Glu	Glu	Ile	Ala 90	Asp	Asn	Glu	Gly	Gly 95	Lys
	Asp	Val	Ser	Met 100	Phe	Pro	Gly	Leu	Ser 105	Asn	Asp	Ser	Asp	Val 110	Lys	Phe
25	His	Glu	Gly 115	Glu	Lys	Gly	Glu	Asp 120	Pro	Tyr	Ile	Ser	Leu 125	Pro	Asn	Gln
	Glu	Asp 130	Ser	Gln	Glu	Glu	Lys 135	Gln	Glu	Leu	Gln	Val 140	Tyr	Pro	Ser	Asp
30	Asn 145	Leu	Val	Leu	Ala	Ala 150	Arg	Thr	Glu	Asp	Asp 155	Val	Ser	Tyr	Leu	Asp 160
35	Ile	Tyr	Val	Tyr	Asp 165	Asp	Gly	Ala	Gly	Phe 170	His	Ser	Ser	Asp	Ile 175	Pro
	Val	Glu	Glu	Gly 180	Asp	Glu	Ala	Asp	Pro 185	Asp	Val	Ala	Arg	Gly 190	Leu	Val
40	Arg	Asp	Pro. 195	Ala	Leu	Tyr	Val	His 200	His	Asp	Leu	Met	Leu 205	Pro	Ala	Phe
	Pro	Leu 210	_	Val	Glu	Trp	Leu 215	Asp	Tyr	Lys	Val	Gly 220	Ser	Asn	Ser	Glu
45	Glu 225		Ala	Asn	Tyr	Ala 230	Ala	Ile	Gly	Thr	Phe 235	Asp	Pro	Gln	Ile	Glu 240

- 142 -

	Ile	Trp	Asn	Leu	Asp 245	Cys	Val	Asp	Lys	Ala 250	Phe	Pro	Asp	Met	Ile 255	Leu
5	Gly	Glu	Pro	Leu 260	Asp	Asn	Ser	Met	Val 265	Ser	Leu	Lys	Ser	Lys 270	Lys	Lys
	Lys	Lys	Lys 275	Ser	Lys	Thr	Gly	His 280	Ile	Thr	Thr	His	His 285	Thr	Asp	Ala
10	Val	Leu 290	Ser	Met	Ala	His	Asn 295	Lys	Tyr	Phe	Arg	Ser 300	Val	Leu	Ala	Ser
15	Thr 305	Ser	Ala	Asp	His	Thr 310	Val	Lys	Leu	Trp	Asp 315	Leu	Asn	Ser	Gly	Asn 320
	Ala	Ala	Arg	Ser	Leu 325	Ala	Ser	Ile	His	Ser 330	Asn	Lys	Asn	Val	Ser 335	Ser
20	Ser	Glu	Trp	His 340	Met	Leu	Asn	Gly	Ser 345	Ile	Leu	Leu	Thr	Gly 350	Gly	Tyr
	Asp	Ser	Arg 355	Val	Ala	Leu	Thr	Asp 360	Val	Arg	Ile	Ser	Asp 365	Glu	Ser	Gln
25	Met	Ser 370	Lys	Tyr	Trp	Ser	Ala 375	Met	Ala	Gly	Glu	Glu 380	Ile	Glu	Thr	Val
30	385					390				_	395		-		Gly	400
					405					410					Val 415	
35				420					425		٠		-	430	Asn	_
40			435					440				-	445	•	Thr	
40		450					455					460		-	Gly	
45	465					470	_		_		475				Thr	480
					ىرىد-			- 41		y					y	1

- 143 -

Val Asn Lys Val Leu Lys Leu Trp Asp Val Phe Thr Asn Arg Ser Val Arg Lys Ser Phe Lys Ser Glu Leu Glu Asn Val Gln Ala Arg Ala Lys Glu Glu Ala Gln Lys Ile Gly Lys Ser Ser Arg Ile Ala Arg Lys Tyr Thr Ser Asn Asp Asn Pro Asp Thr Val Ile Thr Ile Asp Asp Gln Gly Glu Asp Glu Glu Glu Arg Glu Gly Gly Asp Glu His Asp Asp Met Ala (2) INFORMATION FOR SEQ ID NO:57: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 325 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP, Fig. 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:57: Met His Tyr Met Ser Gly His Ser Asn Phe Val Ser Tyr Val Cys Ile Ile Pro Ser Ser Asp Ile Tyr Pro His Gly Leu Ile Ala Thr Gly Gly Asn Asp His Asn Ile Cys Ile Phe Ser Leu Asp Ser Pro Met Pro Leu

- 144 -

	Tyr	Ile 50	Leu	Lys	Gly	His	Lys 55	Asp	Thr	Val	Cys	Ser 60	Leu	Ser	Ser	Gly
5	Lys 65	Phe	Gly	Thr	Leu	Leu 70	Ser	Gly	Ser	Trp	Asp 75	Thr	Thr	Ala	Lys	Val 80
	Trp	Leu	Asn	Asp	Lys 85	Cys	Met	Met	Thr	Leu 90	Gln	Gly	His	Thr	Ala 95	Ala
10	Val	Trp	Ala	Val 100	Lys	Ile	Leu	Pro	Glu 105	Gln	Gly	Leu	Met	Leu 110	Thr	Gly
. 15	Ser	Ala	Asp 115	Lys	Thr	Ile	Lys	Leu 120	Trp	Lys	Ala	Gly	Arg 125	Суз	Glu	Arg
	Thr	Phe 130	Leu	Gly	His	Glu	Asp 135	Cys	Val	Arg	Gly	Leu 140	Ala	Ile	Leu	Ser
20	Glu 145	Thr	Glu	Phe	Leu	Ser 150	Cys	Ala	Asn	Asp	Ala 155	Ser	Ile	Arg	Arg	Trp 160
	Gln	Ile	Thr	Gly	Glu 165	Cys	Leu	Glu	Val	Tyr 170	Phe	Gly	His	Thr	Asn 175	Tyr
25	Ile	Tyr	Ser	Ile 180	Ser	Val	Phe	Pro	Asn 185	Ser	Lys	Asp	Phe	Val 190	Thr	Thr
30	Ala	Glu	Asp 195	Arg	Ser	Leu	Arg	Ile 200	Trp	Lys	His	Gly	Glu 205	Cys	Ala	Gln
	Thr	Ile 210	Arg	Leu	Pro	Ala	Gln 215	Ser	Ile	Trp	Cys	Cys 220	Cys	Val	Leu	Glu
35	Asn 225	Gly	Asp	Ile	Val	Val 230	Gly	Ala	Ser	Asp	Gly 235	Ile	Ile	Arg	Val	Phe 240
	Thr	Glu	Ser	Glu	Glu 245	Arg	Thr	Ala	Ser	Ala 250	Glu	Glu	Ile	Lys	Ala 255	Ser
40	Leu	Ser	Arg	Glu 260	Ser	Pro	Leu	Ile	Ala 265	ГÀа	Val	Leu	Thr	Thr 270	Glu	Pro
45	Pro	Ile	Ile 275	Thr	Pro	Val	Arg	Arg 280	Thr	Leu	Pro	Cys	Arg 285	Val	Thr	Arg
	Ser	Met	Ile	Ser	Ser	Cys	Leu	Ser	Arg	Leu	Val	Ser	Thr	Ser	Leu	Ser

- 145 -

295 300 290 Thr Ser Asp Ser His Leu Thr Ile Thr Ala Leu His Leu Phe Leu Thr 310 315 305 5 Thr Thr Thr Thr Glu 325 (2) INFORMATION FOR SEQ ID NO:58: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 425 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown. 15 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -HUMAN, Fig. 41 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:58: Met Ala Asp Lys Glu Ala Ala Phe Asp Asp Ala Val Glu Glu Arg Val 10 30 5 Ile Asn Glu Glu Tyr Lys Ile Trp Lys Lys Asn Thr Pro Phe Leu Tyr 25 20 Asp Leu Val Met Thr His Ala Leu Glu Trp Pro Ser Leu Thr Ala Gln 35 . 35 40 Trp Leu Pro Asp Val Thr Arg Pro Glu Gly Lys Asp Phe Ser Ile His 50 40 Arg Leu Val Leu Gly Thr His Thr Ser Asp Glu Gln Asn His Leu Val

70

85

65

45

75

90

Ile Ala Ser Val Gln Leu Pro Asn Asp Asp Ala Gln Phe Asp Ala Ser

80

95

- 146 -

	His	Tyr	Asp	Ser		Lys	Gly	Glu	Phe 105		Gly	Phe	Gly	Ser		. Ser
. 5	Gly	Lys	Ile 115	Glu	Ile	Glu	Ile	Lys 120	Ile	Asn	His	Glu	Gly 125		Val	Asn
	Arg	Ala 130		Tyr	Met	Pro	Gln 135	Asn	Pro	Суз	Ile	Ile 140		Thr	Lys	Thr
10	Pro 145		Ser	Asp	Val	Leu 150	Val	Phe	Asp	Tyr	Thr 155	Lys	His	Pro	Ser	Lys 160
15	Pro	Asp	Pro	Ser	Gly 165	Glu	Cys	Asn	Pro	Asp 170	Leu	Arg	Leu	Arg	Gly 175	His
	Gln	Lys	Glu	Gly 180	Tyr	Gly	Leu	Ser	Trp 185	Asn	Pro	Asn	Leu	Ser 190	Gly	His
20	Leu	Leu	Ser 195	Ala	Ser	Asp	Asp	His 200	Thr	Ile	Cys	Leu	Trp 205	Asp	Ile	Ser
	Ala	Val 210	Pro	Lys	Glu	Gly	Lys 215	Val	Val	Asp	Ala	Lys 220	Thr	Ile	Phe	Thr
25	Gly 225	His	Thr	Ala	Val	Val 230	Glu	Asp	Val	Ser	Trp 235	His	Leu	Leu	His	Glu 240
30	Ser	Leu	Phe	Gly	Ser 245	Val	Ala	Asp	Asp	Gln 250	Lys	Leu	Met	Ile	Trp 255	Asp
	Thr	Arg	Ser	Asn 260	Asn	Thr	Ser	Lys	Pro 265	Ser	His	Ser	Val	Asp 270	Ala	His
35			Glu 275					280					285			
,		290	Thr				295					300		_		_
40	305		Lys			310					315					320
45			Val		325					330					335	
	Gly	Thr	Asp	Arg	Arg	Leu	Asn	Val	Trp	Asp	Leu	Ser	Lys	Ile	Gly	Glu

- 147 -

345 350 340 Glu Gln Ser Pro Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe 355 5 Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro 375 370 Asn Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln 395 390 10 385 Val Trp Gln Met Ala Glu Asn Ile Tyr Asn Asp Glu Asp Pro Glu Gly 415 410 405 Ser Val Asp Pro Glu Gly Gln Gly Ser 425 420 (2) INFORMATION FOR SEQ ID NO:59: (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 852 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 30 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: S253 PROTEIN, Fig. 42 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59: 35 Met Phe Lys Ser Lys Thr Ser Thr Leu Ser Tyr Asp Glu Thr Pro Asn 10 Ser Asn Glu Gly Asp Arg Asn Ala Thr Pro Val Asn Pro Lys Glu Lys 40 25 20 Ser Gln Thr Lys His Leu Asn Ile Pro Gly Asp Arg Ser Arg His Ser 35 40 45 Ser Ile Ala Asp Ser Lys Arg Ser Ser Ser Arg Tyr Asp Gly Gly Tyr

- 148 -

		50					55					60				
	Ser 65	Ala	Asp	Ile	Ile	Pro 70	Ala	Gln	Leu	Arg	Phe 75	Ile	Asp	Asn	Ile	Asp 80
J	Tyr	Gly	Thr	Arg	Leu 85	Arg	Lys	Thr	Leu	His 90	Arg	Asn	Ser	Val	Val 95	Ser
10	Asn	Gly	Tyr	Asn 100	Lys	Leu	Ser	Glu	Asn 105	Asp	Arg	Trp	Tyr	Phe 110	Asp	Leu
	Phe	Asp	Arg 115	Lys	Tyr	Phe	Glu	Asn 120	Tyr	Leu	Glu	Glu	Pro 125	Thr	Tyr	Ile
15	Lys	Ile 130	Phe	Lys	Lys	Lys	Glu 135	Gly	Leu	Glu	Gln	Phe 140	Asp	Arg	Met	Phe
20	Leu 145	Ala	Gln	Glu	Leu	Lys 150	Ile	Pro	Asp	Val	Tyr 155	Lys	Ser	Thr	Thr	Tyr 160
20	Gl'n	Gly	Glu	Pro	Ala 165	Val	Ala	Asn	Ser	Glu 170	Leu	Phe	Lys	Asn	Ser 175	Ile
25	Cys	Cys	Cys	Thr 180	Phe	Ser	His	Asp	Gly 185	Lys	Tyr	Met	Val	Ile 190	Gly	Cys
	Lys	Asp	Gly 195	Ser	Leu	His	Leu	Trp 200	Lys	Val	Ile	Asn	Ser 205	Pro	Val	Lys ·
30	Arg	Ser 210	Glu	Met	Gly	Arg	Ser 215	Glu	Lys	Ser	Val	Ser 220	Ala	Ser	Arg	Ala
35	Asn 225	Ser	Leu	Lys	Ile	Gln 230	Arg	His	Leu	Ala	Ser 235	Ile	Ser	Ser	His	Asn 240
	Gly	Ser	Ile	Ser	Ser 245	Asn	Asp	Leu	Lys	Pro 250	Ser	Asp	Gln	Phe	Glu 255	Gly
40	Pro	Ser	Lys	Gln 260	Leu	His	Leu	Tyr	Ala 265	Pro	Val	Phe	Tyr	Ser 270	Asp	Val
	Phe	Arg	Val 275	Phe	Met	Glu	His	Ala 280	Leu	Asp	Ile	Leu	Asp 285	Ala	Asn	Trp
45	Ser	Lys 290	Asn	Gly	Phe	Leu	Ile 295	Thr	Ala	Ser	Met	Asp 300	Lys	Thr	Ala	Lys

- 149 -

	L u 305	Trp	His	Pro	Glu	Arg 310	Lys	Tyr	Ser	Leu	Lys 315	Thr	Phe	Val	His	Pro 320
5	Asp	Phe	Val	Thr	Ser 325	Ala	Ile	Phe	Phe	Pro 330	Asn	Asp	Asp	Arg	Phe 335	Ile
	Ile	Thr	Gly	Cys 340	Leu	Asp	His	Arg	Cys 345	Arg	Leu	Trp	Ser	Ile 350	Leu	Asp
10	Asn	Glu	Val 355	Ser	Tyr	Ala	Phe	Asp 360	Cys	Lys	Asp	Leu	Ile 365	Thr	Ser	Leu
15	Thr	Leu 370	Ser	Pro	Pro	Gly	Gly 375	Glu	Tyr	Thr	Ile	Ile 380	Gly	Thr	Phe	Asn
	Gly 385	Tyr	Ile	Tyr	Val	Leu 390	Leu	Thr	His	Gly	Leu 395	Lys	Phe	Val	Ser	Ser 400
20	Phe	His	Val	Ser	Asp 405	Lys	Ser	Thr	Gln	Gly 410	Thr	Thr	Lys	Asn	Ser 415	Phe
	His	Pro	Ser	Ser 420		Tyr	Gly	Lys	Val 425	Gln	His	Gly	Pro	Arg 430	Ile	Thr
25	Gly	Leu	Gln 435	Суѕ	Phe	Phe	Ser	Lys 440	Val	Asp	Lys	Asn	Leu 445	Arg	Leu	Ile
30	Val	Thr 450	Thr	Asn	Asp	Ser	Lys 455		Gln	Ile	Phe	Asp 460	Leu	Asn	Glu	Lys
	Lys 465	Pro	Leu	Glu	Leu	Phe 470	Lys	Gly	Phe	Gln	Ser 475	Gly	Ser	Ser	Arg	His 480
35	Arg	Gly	Gln	Phe	Leu 485	Met	Met	Lys	Asn	Glu 490	Pro	Val	Val	Phe	Thr 495	Gly
	Ser	Asp	Asp	His 500	_	Phe	Tyr	Thr	Trp 505	Lys	Met	Gln	Ser	Phe 510	Asn	Leu
40	Ser	Ala	Glu 515		Asn	Cys	Thr	Ala 520		His	Arg	Lys	Lys 525	Arg	Leu	Ser
45	Gly	Ser 530		Ser	Leu	Lys	Gly 535		Leu	Arg	Ile	Val 540	Ser	Asn	Lys	Ser
	Thr	. Asr	Asp	Glu	суя	Lev	Thr	Glu	Thr	Ser	Asn	Gln	Ser	Ser	Ser	His

- 150 -

	545					550					555					560
5	Thr	Phe	Thr	Asn	Ser 565	Ser	Lys	Asn	Val	Leu 570	Gln	Thr	Gln	Thr	Val 575	Gly
J	Ser	Gln	Ala	Ile 580	Lys	Asn	Asn	His	Tyr 585	Ile	Ser	Phe	His	Ala 590	His	Asn
10	Ser	Pro	Val 595	Thr	Cys	Ala	Ser	Ile 600	Ala ·	Pro	Asp	Val	Ala 605	Ile	Lys	Asn
	Leu	Ser 610	Leu	Ser	Asn	Asp	Leu 615	Ile	Phe	Glu	Leu	Thr 620	Ser	Gln	Tyr	Phe
15	Lys 625	Glu	Met	Gly	Gln	Asn 630	Tyr	Ser	Glu	Ser	Lys 635	Glu	Thr	Cys	Asp	Asn 640
20	Lys	Pro	Asn	His	Pro 645	Val	Thr	Glu	Thr	Gly 650	Gly	Phe	Ser	Ser	Asn 655	Leu
	Ser	Asn	Val	Val 660	Asn	Asn	Val	Gly	Thr 665	Ile	Leu	Ile	Thr	Thr 670	Asp	Ser
25	Gln	Gly	Leu 675	Ile	Arg	Val	Phe	Arg 680	Thr	Asp	Ile	Leu	Pro 685	Glu	Ile	Arg
	Lys	Lys 690	Ile	Ile	Glu	Lys	Phe 695	His	Glu	Tyr	Asn	Leu 700	Phe	His	Leu	Glu
30	Ala 705	Ala	Gly	Lys	Ile	Asn 710	Asn	His	Asn	Asn	Asp 715	Ser	Ile	Leu	Glu	Asn 720
35	Arg	Met	Asp	Glu	Arg 725	Ser	Ser	Thr	Glu	Asp 730	Asn	Glu	Phe	Ser	Thr 735	Thr
	Pro	Pro	Ser	Asn 740	Thr	His	Asn	Ser	Arg 745	Pro	Ser	His	Asp	Phe 750	Cys	Glu
40	Leu	His	Pro 755	Asn	Asn	Ser	Pro	Val 760	Ile	Ser	Gly	Met	Pro 765	Ser	Arg	Ala
	Ser	Ala 770	Ile	Phe	Lys	Asn	Ser 775	Ile	Phe	Asn	Lys	Ser 780	Asn	Gly	Ser	Phe
45	Ile 785	Ser	Leu	Lys	Ser	Arg	Ser	Glu	Ser	Thr	Ser	Ser	Thr	Val	Phe	Gly 800

- 151 -

Pro His Asp Ile Pro Arg Val Ser Thr Thr Tyr Pro Lys Leu Lys Cys 805 810 Asp Val Cys Asn Gly Ser Asn Phe Glu Cys Ala Ser Lys Asn Pro Ile 825 5 Ala Gly Gly Asp Ser Gly Phe Thr Cys Ala Asp Cys Gly Thr Ile Leu 845 840 Asn Asn Phe Arg 10 850 (2) INFORMATION FOR SEQ ID NO:60: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 488 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: SOF1, Fig. 43 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60: Met Lys Ile Lys Thr Ile Lys Arg Ser Ala Asp Asp Tyr Val Pro Val 5 1 10 35 Lys Ser Thr Gln Glu Ser Gln Met Pro Arg Asn Leu Asn Pro Glu Leu 20 25 His Pro Phe Glu Arg Ala Arg Glu Tyr Thr Lys Ala Leu Asn Ala Thr 35 40 Lys Leu Glu Arg Met Phe Ala Lys Pro Phe Val Gly Gln Leu Gly Tyr 50 55 60 Gly His Arg Asp Gly Val Tyr Ala Ile Ala Lys Asn Tyr Gly Ser Leu 65 70 75 45

- 152 -

	Asn	Lys	Leu	Ala	Thr 85	Gly	Ser	Ala	Asp	Gly 90	Val	Ile	Lys	Туг	Trp 95) Asn	
5	Met	Ser	Thr	Arg 100		Glu	Phe	Val	Ser		Lys	Ala	His	Tyr 110	_	Leu	
	Val	Thr	Gly 115	Leu	Cys	Val	Thr	Gln 120	Pro	Arg	Phe	His	Asp 125		Lys	Pro	
10	Asp	Leu 130	Lys	Ser	Gln	Asn	Phe 135	Met	Leu	Ser	Cys	Ser 140	Asp	Asp	Lys	Thr	
15	Val 145		Leu	Trp	Ser	Ile 150	Asn	Val	Asp	Asp	Tyr 155	Ser	Asn	Lys	Asn	Ser 160	
	Ser	Asp	Asn	Asp	Ser 165	Val	Thr	Asn	Glu	Glu 170	Gly	Leu	Ile	Arg	Thr 175	Phe	•
20	Asp	Gly	Glu	Ser 180	Ala	Phe	Gln	Gly	Ile 185	Asp	Ser	His	Arg	Glu 19 0	Asn	Ser	
	Thr	Phe	Ala 195	Thr	Gly	Gly	Ala	Lys 200	Ile	His	Leu	Trp	Asp 205	Val	Asn	Arg	
25	Leu	Lys 210	Pro	Val	Ser	Asp	Leu 215	Ser	Trp	Gly	Ala	Asp 220	Asn	Ile	Thr	Ser	
30	Leu 225	Lys	Phe	Asn	Gln	Asn 230	Glu	Thr	Asp	Ile	Leu 235	Ala	Ser	Thr	Gly	Ser 240	
	Asp	Asn	Ser	Ile	Val 245	Leu	Tyr	Asp	Leu	Arg 250	Thr	Asn	Ser	Pro	Thr 255	Gln	
35	Lys	Ile	Val	Gln 260	Thr	Met	Arg	Thr	Asn 265	Ala	Ile	Cys	Trp	Asn 270	Pro	Met	
	Glu	Ala	Phe 275	Asn	Phe	Val	Thr	Ala 280	Asn	Glu	Asp		Asn 285	Ala	Tyr	Tyr	
40	Tyr	Asp 290	Met	Arg	Asn	Leu	Ser 295	Arg	Ser	Leu	Asn	Val 300	Phe	Lys	Asp	His	
45	Val 305	Ser	Ala	Val	Met	Asp 310	Val	Asp	Phe	Ser	Pro 315	Thr	Gly	Asp	Glu	Ile 320	
	Val	Thr	Gly	Ser	Tyr	Asp	Lys	Ser	Ile	Arg	Ile	Tyr	Lys	Thr	Asn	His	

- 153 -

Gly His Ser Arg Glu Ile Tyr His Thr Lys Arg Met Gln His Val Phe Val Lys Tyr Ser Met Asp Ser Lys Tyr Ile Ile Ser Gly Ser Asp Asp Gly Asn Val Arg Leu Trp Arg Ser Lys Ala Trp Glu Arg Ser Asn Val Lys Thr Thr Arg Glu Lys Asn Lys Leu Glu Tyr Asp Glu Lys Leu Lys Glu Arg Phe Arg His Met Pro Glu Ile Lys Arg Ile Ser Arg His Arg His Val Pro Gln Val Ile Lys Lys Ala Gln Glu Ile Lys Asn Ile Glu Leu Ser Ser Ile Lys Arg Arg Glu Ala Asn Glu Arg Arg Thr Arg Lys Asp Met Pro Tyr Ile Ser Glu Arg Lys Lys Gln Ile Val Gly Thr Val His Lys Tyr Glu Asp Ser Gly Arg Asp Arg Lys Arg Arg Lys Glu Asp Asp Lys Arg Asp Thr Gln Glu Lys (2) INFORMATION FOR SEQ ID NO:61: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 423 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- 154 -

(C) INDIVIDUAL ISOLATE: STE4 - YEAST, Fig. 44

5	(xi)	SEQ	JENCI	E DES	SCRII	PTIO	N: SI	EQ II	ои с	:61:							•
-	Met 1	Ala	Ala	His	Gln 5	Met	Asp	Ser	Ile	Thr 10	Tyr	Ser	Àsn	Asn	Val 15	Thr	<u>,</u>
10	Gln	Gln	Tyr	Ile 20	Gln	Pro	Gln	Ser	Leu 25	Gln	Asp	Ile	Ser	Ala 30	Val	Glu	
	Asp	Glu	Ile 35	Gln	Asn	Lys	Ile	Glu 40	Ala	Ala	Arg	Gln	Glu 45	Ser	Lys	Gln	
15	Leu	His 50	Ala	Gln	Ile	Asn	Lys 55	Ala	Lys	His	Lys	Ile 60	Gln	Asp	Ala	Ser	
•	Leu 65	Phe	Gln	Met	Ala	Asn 70	Lys	Val	Thr	Ser	Leu 75	Thr	Lys	Asn	Lys	Ile 80	
20	Asn	Leu	Lys	Pro	Asn 85	Ile	Val	Leu	Lys	Gly 90	His	Asn	Asn	Lys	Ile 95	Ser	
25	Asp	Phe	Arg	Trp 100	Ser	Arg	Asp	Ser	Lys 105	Arg	Ile	Leu	Ser	Ala 110	Ser	Gln	
	Asp	Gly	Phe 115	Met	Leu	Ile	Trp	Asp 120	Ser	Ala	Ser	Gly	Leu 125	Lys	Gln	Asn	
30	Ala	Ile 130	Pro	Leu	Asp	Ser	Gln 135	Trp	Val	Leu	Ser	Cys 140	Ala	Ile	Ser	Pro	
35	Ser 145	Ser	Thr	Leu	Val	Ala 150	Ser	Ala	Gly	Leu	Asn 155	Asn	Asn	Cys	Thr	Ile 160	
33	Tyr	Arg	Val	Ser	Lys 165	Glu	Asn	Arg	Val	Ala 170	Gln	Asn	Val	Ala	Ser 175	Ile	
40	Phe	Lys	Gly	His 180	Thr	Cys	Tyr	Ile	Ser 185	Asp	Ile	Glu	Phe	Thr 190	Asp	Asn	
	Ala	His	Ile 195	Leu	Thr	Ala	Ser	Gly 200	Asp	Met	Thr	Cys	Ala 205	Leu	Trp	Asp	
45	Ile	Pro 210	Lys	Ala	Lys	Arg	Val 215	Arg	Glu	Tyr	Ser	Asp 220	His	Leu	Gly	Asp	

- 155 -

	Va . 22		Leu	Ala	Leu	Ala	Ile 230	Pro	Glu	Glu	Pro	Asn 235	Leu	Glu	Asn	Ser	Ser 240
5	As	m	Thr	Phe	Ala	Ser 245	Cys	Gly	Ser	Asp	Gly 250	Tyr	Thr	Tyr	Ile	Trp 255	Asp
	Se	er	Arg	Ser	Pro 260	Ser	Ala	Val	Gln	Ser 265	Phe	Tyr	Val	Asn	Asp 270	Ser	Asp
10		Le	Asn	Ala 275	Leu	Arg	Phe	Phe	Lys 280	Asp	Gly	Met	Ser	Ile 285	Val	Ala	Gly
15	Se	er	Asp 290	Asn	Gly	Ala	Ile	Asn 295	Met	Tyr	Asp	Leu	Arg 300	Ser	Asp	Cys	Ser
15		le 05	Ala	Thr	Phe	Ser	Leu 310	Phe	Arg	Gly	Tyr	Glu 315	Glu	Arg	Thr	Pro	Thr 320
20	P :	ro	Thr	Tyr	Met	Ala 325	Ala	Asn	Met	Glu	Tyr 330	Asn	Thr	Ala	Gln	Ser 335	Pro
	G:	ln	Thr	Leu	Lys 340	Ser	Thr	Ser	Ser	Ser 345	Tyr	Leu	Asp	Asn	Gln 350	Gly	Val
25	V	al	Ser	Leu 355	Asp	Phe	Ser	Ala	Ser 360	Gly	Arg	Leu	Met	Tyr 365	Ser	Cys	Tyr
30	T	hr	Asp 370		Gly	Cys	Val	Val 375	Trp	Asp	Val	Leu	Lys 380	Gly	Glu	Ile	Val
30		1y 85	-	Leu	Glu	Gly	His 390	_	Gly	Arg	Val	Thr 395		Val	Arg	Ser	Ser 400
35	P	ro	Asp	Gly	Leu	Ala 405	Val	Cys	Thr	Gly	Ser	Trp	Asp	Ser	Thr	Met 415	Lys
	I	le	Trp	Ser	Pro 420	Gly	Tyr	Gln									
40	(2) IN	FO	RMAT	ON	FOR	SEQ	ID N	0:62	:								
	(i)	SEQ	UENC	E CH	IARAC	TERI	STIC	: :								

(A) LENGTH: 704 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

45

- 156 -

	(ii)	MOLE	CULE	TYP	E: p	rote	in									
	(iii)	нурс	THEI	CICAL	: NO	•										
5	(iv)	ANTI	-SEN	ISE:	ио											
	(vi)						ATE :	TRA	N SCF	RIPTI	ON F	FACTO	OR TI	IF,	Fig.	4!
10	(xi)	SEQU	JENCE	DES	CRIP	OIT	1: SE	Q II	NO:	62:						
	Met 1	Ser	Leu	Glu	Val 5	Ser	Asn	Ile	Asn	Gly 10	Gly	Asn	Gly	Thr	Gln 15	Lei
15	Ser	His	Asp	Lys 20	Arg	Glu	Leu	Leu	Cys 25	Leu	Leu	Lys	Leu	Ile 30	Lys	Ly
20	Tyr	Gln	Leu 35	Lys	Ser	Thr	Glu	Glu 40	Leu	Leu	Cys	Gln	Glu 45	Ala	Asn	Va:
	Ser	Ser 50	Val	Glu	Leu	Ser	Glu 55	Ile	Ser	Glu	Ser	Asp 60	Val	Gln	Gln	Va:
25	Leu 65	Gly	Ala	Val	Leu	Gly 70	Ala	Gly	Asp	Ala	Asn 75	Arg	Glu	Arg	Lys	Hi:
30	Val	Gln	Ser	Pro	Ala 85	Gln	Gly	His	Lys	Gln 90	Ser	Ala	Val	Thr	Glu 95	Ala
	Asn	Ala	Ala	Glu 100	Glu	Leu	Ala	Lys	Phe 105	Ile	Asp	Asp	Asp	Ser 110	Phe	As
35	Ala	Gln	His 115	Tyr	Glu	Gln	Ala	Tyr 120	Lys	Glu	Leu	Arg	Thr 125	Phe	Val	Gli
	Asp	Ser 130	Leu	Asp	Ile	Tyr	Lys 135	His	Glu	Leu	Ser	Met 140	Val	Leu	Tyr	Pr
40	Ile 145	Leu	Val	Gln	Ile	Tyr 150	Phe	Lys	Ile	Leu	Ala 155	Ser	Gly	Leu	Arg	G1 16
	Lys	Ala	Lys	Glu	Phe 165		Glu	Lys	Tyr	Lys 170	Cys	Asp	Leu	Asp	Gly 175	ту

45

- 157 ~

	Tyr	Ile	Glu	Gly 180	Leu	Phe	Asn	Leu	Leu 185	Leu	Leu	Ser	Lys	Pro 190	Glu	Glu
5	Leu	Leu	Glu 195	Asn	Asp	Leu	Val	Val 200	Ala	Met	Glu	Gln	Asp 205	Lys	Phe	Val
	Ile	Arg 210	Met	Ser	Arg	Asp	Ser 215	His	Ser	Leu	Phe	Lys 220	Arg	His	Ile	Gln
10	Asp 225	Arg	Arg	Gln	Glu	Val 230	Val	Ala	Asp	Ile	Val 235	Ser	Lys	Tyr	Leu	His 240
15	Phe	Asp	Thr	Tyr	Glu 245	Gly	Met	Ala	Arg	Asn 250	Lys	Leu	Gln	Cys	Val 255	Ala
	Thr	Ala	Gly	Ser 260	His	Leu	Gly	Glu	Ala 265	Lys	Arg	Gln	Asp	Asn 270	Lys	Met
20	Arg	Val	Tyr 275	Tyr	Gly	Leu	Leu	Lys 280	Glu	Val	Asp	Phe	Gln 285	Thr	Leu	Thr
	Thr	Pro 290	Ala	Pro	Ala	Pro	Glu 295	Glu	Glu	Asp	Asp	Asp 300	Pro	Asp	Ala	Pro
25	Asp 305	Arg	Pro	Lys	Lys	Lys 310	Lys	Pro	Lys	Lys	Asp 315	Pro	Leu	Leu	Ser	Lys 320
30	Lys	Ser	Lys	Ser	Asp 325	Pro	Asn	Ala	Pro	Ser 330	Ile	Asp	Arg	Ile	Pro 335	Leu
	Pro	Glu	Leu	Lys 340	Asp	Ser	Asp		Leu 345	Leu	Lys	Leu	Lys	Ala 350	Leu	Arg
35	Glu	Ala	Ser 355	Lys	Arg	Leu	Ala	Leu 360	Ser	Lys	Asp	Gln	Leu 365	Pro	Ser	Ala
	Val	Phe 370	Tyr	Thr	Val	Leu	Asn 375	Ser	His	Gln	Gly	Val 380	Thr	Cys	Ala	Glu
40	Ile 385	Ser	Asp	Asp	Ser	Thr 390	Met	Leu	Ala	Cys	Gly 395	Phe	Gly	Asp	Ser	Ser 400
45	Val	Arg	Ile	Trp	Ser 405	Leu	Thr	Pro	Ala	Asn 410	Val	Arg	Thr	Leu	Lys 415	Asp
	Ala	Asp	Ser	Leu	Arg	Glu	Leu	Asp	Lys	Glu	Ser	Ala	Asp	Ile	Asn	Val

- 158 **-**

				420					425					430		
5	Arg	Met	Leu 435	Asp	Asp	Arg	Ser	Gly 440	Glu	Val	Thr	Arg	Ser 445	Leu	Met	Gly
•	His	Thr 450	Gly	Pro	Val	Tyr	Arg 455	Cys	Ala	Phe	Ala	Pro 460	Glu	Met	Asn	Leu
10	Leu 465	Leu	Ser	Cys	Ser	Glu 470	Asp	Ser	Thr	Ile	Arg 475	Leu	Trp	Ser	Leu	Leu 480
	Thr	Trp	Ser	Cys	Val 485	Val	Thr	Tyr	Arg	Gly 490	His	Val	Tyr	Pro	Val 495	Trp
15	Asp	Val	Arg	Phe 500	Ala	Pro	His	Gly	Tyr 505	Tyr	Phe	Val	Ser	Cys 510	Ser	Tyr
20	Asp	Lys	Thr 515	Ala	Arg	Leu	Trp	Ala 520	Thr	Asp	Ser	Asn	Gln 525	Ala	Leu	Arg
	Val	Phe 530	Val	Gly	His	Leu	Ser 535	Asp	Val	Asp	Cys	Val 540	Gln	Phe	His	Pro
25	Asn 545	Ser	Asn	Tyr	Val	Ala 550	Thr	Gly	Ser	Ser	Asp 555	Arg	Thr	Val	Arg	Leu 560
	Trp	Asp	Asn	Met	Thr 565	Gly	Gln	Ser	Val	Arg 570	Leu	Met	Thr	Gly	His 575	Lys
30	Gly	Ser	Val	Ser 580	Ser	Leu	Ala	Phe	Ser 585	Ala	Cys	Gly	Arg	Tyr 590	Leu	Ala
35	Ser	Gly	Ser 595	Val	Asp	His	Asn	Ile 600	Ile	Ile	Trp	Asp	Leu 605	Ser	Asn	Gly
	Ser	Leu 610	Val	Thr	Thr	Leu	Leu 615	Arg	His	Thr	Ser	Thr 620	Val	Thr	Thr	Ile
40	625					630					635		_		Asp	640
	Asn	Leu	Thr	Leu	Trp 645	Asp	Phe	His	Lys	Val 650	Thr	Glu	qaA	Tyr	Ile 655	Ser
45	Asn	His	Ile	Thr 660		Ser	His				Glu				Asp	Val

- 159 -

Tyr Leu Met Arg Thr Phe Pro Ser Lys Asn Ser Pro Phe Val Ser Leu 675 680 685

His Phe Thr Arg Arg Asn Leu Leu Met Cys Val Gly Leu Phe Lys Ser 690 695 700

- (2) INFORMATION FOR SEQ ID NO:63:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 713 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: protein
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1, Fig. 46
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met Thr Ala Ser Val Ser Asn Thr Gln Asn Lys Leu Asn Glu Leu Leu 1 5 10 15

Asp Ala Ile Arg Gln Glu Phe Leu Gln Val Ser Gln Glu Ala Asn Thr 20 25 30

Tyr Arg Leu Gln Asn Gln Lys Asp Tyr Asp Phe Lys Met Asn Gln Gln 35 40 45

. 35

Leu Ala Glu Met Gln Gln Ile Arg Asn Thr Val Tyr Glu Leu Glu Leu 50 55 60

Thr His Arg Lys Met Lys Asp Ala Tyr Glu Ala Glu Ile Lys His Leu 40 65 70 75 80

Lys Leu Gly Leu Glu Gln Arg Asp His Gln Ile Ala Ser Leu Thr Val 85 90 95

- 160 -

	Gln	Gln	Gln 115	Gln	Gln	Gln	Leu	Ala 120	Ala	Ala	Ser	Ala	Ser 125	Val	Pro	Val
5	Ala	Gln 130	Gln	Pro	Pro	Ala	Thr 135	Thr	Ser	Ala	Thr	Ala 140	Thr	Pro	Ala	Ala
	Asn 145	Thr	Thr	Thr	Gly	Ser 150	Pro	Ser	Ala	Phe	Pro 155	Val	Gln	Ala	Ser	Arg 160
10	Pro	Asn	Leu	Val	Gly 165	Ser	Gln	Leu	Pro	Thr 170	Thr	Thr	Leu	Pro	Val 175	Val
15	Ser	Ser	Asn	Ala 180	Gln	Gln	Gln	Leu	Pro 185	Gln	Gln	Gln	Leu	Gln 190	Gln	Gln
13	Gln	Leu	Gln 195	Gln	Gln	Gln	Pro	Pro 200	Pro	Gln	Val	Ser	Val 205	Ala	Pro	Leu
20	Ser	Asn 210	Thr	Ala	Ile	Asn	Gly 215	Ser	Pro	Thr	Ser	Lys 220	Glu	Thr	Thr	Thr
	Leu 225	Pro	Ser	Val	Lys	Ala 230	Pro	Glu	Ser	Thr	Leu 235	Lys	Glu	Thr	Glu	Pro 240
25	Glu	Asn	Asn	Asn	Thr 245	Ser	Lys	Ile	Asn	Asp 250	Thr	Gly	Ser	Ala	Thr 255	Thr
30	Ala	Thr	Thr	Thr 260	Thr	Ala	Thr	Glu	Thr 265	Glu	Ile	Lys	Pro	Lys 270	Glu	Glu
	Asp	Ala	Thr 275	Pro	Ala	Ser	Leu	His 280	Gln	Asp	His	Tyr	Leu 285	Val	Pro	Tyr
35		Gln 290	Arg	Ala	Asn	His	Ser 295	Lys	Pro	Ile	Pro	Pro 300	Phe	Leu	Leu	Ąap
	Leu 305	Asp	Ser	Gln	Ser	Val 310	Pro	Asp	Ala	Leu	Lys 315	Lys	Gln	Thr	Asn	Asp 320
40	Tyr	Tyr	Ile	Leu	Tyr 325	Asn	Pro	Ala	Leu	Pro 330	Arg	Glu	Ile	Asp	Val 335	Glu
45	Leu	His	Lys	Ser 340	Leu	Asp	His	Thr	Ser 345	Val	Val	Cys	Cys	Val 350	Lys	Phe
	Ser	Asn	Asp	Gly	Glu	Tyr	Leu	Ala	Thr	Gly	Cys	Asn	Lys	Thr	Thr	Gln

- 161 -

			355					360					365			
	Val	Tyr 370	Arg	Val	Ser	Asp	Gly 375	Ser	Leu	Val	Ala	Arg 380	Leu	Ser	Asp	Asp
5	Ser 385	Ala	Ala	Asn	Asn	His 390	Arg	Asn	Ser	Ile	Thr 395	Glu	Asn	Asn	Thr	Thr 400
10	Thr	Ser	Thr	_	Asn 405	Asn	Thr	Met	Thr	Thr 410	Thr	Thr	Thr	Thr	Thr 415	Ile
	Thr	Thr	Thr	Ala 420	Met	Thr	Ser	Ala	Ala 425	Glu	Leu	Ala	Lys	Asp 430	Val	Glu
15	Asn	Leu	Asn 435	Thr	Ser	Ser	Ser	Pro 440	Ser	Ser	Asp	Leu	Tyr 445	Ile	Arg	Ser
20	Val	Cys 450	Phe	Ser	Pro	Asp	Gly 455	Lys	Phe	Leu	Ala	Thr 460	Gly	Ala	Glu	Asp
	Arg 465	Leu	Ile	Arg	Ile	Trp 470	Asp	Ile	Glu	Asn	Arg 475	Lys	Ile	Val	Met	Ile 480
25	Leu	Gln	Gly	His	Glu 48 5	Gln	Asp	Ile	Tyr	Ser 490	Leu	Asp	Tyr	Phe	Pro 495	Ser
	Gly	Asp	Lys	Leu 500	Val	Ser	Gly	Ser	Gly 505	Asp	Arg	Thr	Val	Arg 510	Ile	Trp
30	Asp	Leu	Arg 515	Thr	Gly	Gln	Сув	Ser 520	Leu	Thr	Leu	Ser	Ile 525	Glu	Asp	Gly
35	Val	Thr 530	Thr	Val	Ala	Val	Ser 535	Pro	Gly	Asp	Gly	Lys 540	Tyr	Ile	Ala	Ala
	Gly 545	Ser	Leu	Asp	Arg	Ala 550	Val	Arg	Val	Trp	Asp 555	Ser	Glu	Thr	Gly	Phe 560
40	Leu	Val	Glu	Arg	Leu 565	Asp	Ser	Glu	Asn	Glu 570	Ser	Gly	Thr	Gly	His 575	Lys
	Asp	Ser	Val	Tyr 580	Ser	Val	Val	Phe	Thr 585		Asp	Gly	Gln	Ser 590	Val	Val
45	Ser	Gly	Ser 595		Asp	Arg	Ser	Val	_	Leu	Trp	Asn	Leu 605		Asn	Ala

- 162 -

Asn Asn Lys Ser Asp Ser Lys Thr Pro Asn Ser Gly Thr Cys Glu Val 610 615 Thr Tyr Ile Gly His Lys Asp Phe Val Leu Ser Val Ala Thr Thr Gln 5 625 630 635 Asn Asp Glu Tyr Ile Leu Ser Gly Ser Lys Asp Arg Gly Val Leu Phe 645 650 Trp Asp Lys Lys Ser Gly Asn Pro Leu Leu Met Leu Gln Gly His Arg 10 660 665 Asn Ser Val Ile Ser Val Ala Val Ala Asn Gly Ser Ser Leu Gly Pro 675 680 685 15 Glu Tyr Asn Val Phe Ala Thr Gly Ser Gly Asp Cys Lys Ala Arg Ile 700 690 695 Trp Lys Tyr Lys Lys Ile Ala Pro Asn 20 705 710 (2) INFORMATION FOR SEQ ID NO:64: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 798 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG, Fig. 47 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64: 40 Met Ser Gln Lys Gln Ser Thr Asn Gln Asn Gln Asn Gly Thr His Gln 10 Pro Gln Pro Val Lys Asn Gln Arg Thr Asn Asn Ala Ala Gly Ala Asn 45 20 25

- 163 -

	Ser	Gly	Gln 35	Gln	Pro	Gln	Gln	Gln 40	Ser	Gln	Gly	Gln	Ser 45	Gln	Gln	Gln
5	Gly	Arg 50	Ser	Asn	Gly	Pro	Phe 55	Ser	Ala	Ser	Asp	Leu 60	Asn	Arg	Ile	Val
	Leu 65	Glu	Tyr	Leu	Asn	Lys 70	Lys	Gly	Tyr	His	Arg 75	Thr	Glu	Ala	Met	Leu 80
10	Arg	Ala	Glu	Ser	Gly 85	Arg	Thr	Leu	Thr	Pro 90	Gln	Asn	Lys	Gln	Ser 95	Pro
15	Ala	Asn	Thr	Lys 100	Thr	Gly	Lys	Phe	Pro 105	Glu	Gln	Ser	Ser	Ile 110	Pro	Pro
	Asn	Pro	Gly 115	Lys	Thr	Ala	Lys	Pro 120	Ile	Ser	Asn	Pro	Thr 125	Asn	Leu	Ser
20	Ser	Lys 130	Arg	Asp	Ala	Glu	Gly 135	Gly	Ile	Val	Ser	Ser 140	Gly	Arg	Leu	Glu
	Gly 145	Leu	Asn	Ala	Pro	Glu 150	Asn	Tyr	Ile	Arg	Ala 155	Tyr	Ser	Met	Leu	Lys 160
25	Asn	Trp	Val	Asp	Ser 165	Ser	Leu	Glu	Ile	Tyr 170	Lys	Pro	Glu	Leu	Ser 175	Tyr
30	Ile	Met	Tyr	Pro 180	Ile	Phe	Ile	Tyr	Leu 185	Phe	Leu	Asn	Leu	Val 190	Ala	Lys
	Asn	Pro	Val 195	Tyr	Ala	Arg	Arg	Phe 200	Phe	Asp	Arg	Phe	Ser 205	Pro	Asp	Phe
35	Lys	Asp 210	Phe	His	Gly	Ser	Glu 215	Ile	Asn	Arg	Leu	Phe 220	Ser	Val	Asn	Ser
	Ile 225	Asp	His	Ile	Lys	Glu 230	Asn	Glu	Val	Ala	Ser 235	Ala	Phe	Gln	Ser	His 240
40	Lys	Tyr	Arg	Ile	Thr 245	Met	Ser	Lys	Thr	Thr 250	Leu	Asn	Leu	Leu	Leu 255	Tyr
45	Phe	Leu	Asn	Glu 260	Asn	Glu	Ser	Ile	Gly 265	Gly	Ser	Leu	Ile	Ile 270	Ser	Val
	Ile	Asn	Gln	His	Leu	Asp	Pro	Asn	Ile	Val	Glu	Ser	Val	Thr	Ala	Arg

- 164 -

			275					280					285				
5	Glu	Lys 290	Leu	Ala	Asp	Gly	Ile 295	Lys	Val	Leu	Ser	Asp 300	Ser	Glu	Asn	Gly	
5	Asn 305	Gly	Lys	Gln	Asn	Leu 310	Glu	Met	Asn	Ser	Val 315	Pro	Val	Lys	Leu	Gly 320	
10	Pro	Phe	Pro	Lys	Asp 325	Glu	Glu	Phe	Val	Lys 330	Glu	Ile	Glu	Thr	Glu 335	Leu	
	Lys	Ile	Lys	Asp 340	Asp	Gln	Glu	Lys	Gln 345	Leu	Asn	Gln	Gln	Thr 350	Ala	Gly	
15	Asp	Asn	Tyr 355	Ser	Gly	Ala	Asn	Asn 360	Arg	Thr	Leu	Leu	Gln 365	Glu	Tyr	Lys	
20	Ala	Met 370	Asn	Asn	Glu	Lys	Phe 375	Lys	Asp	Asn	Thr	Gly 380	Asp	Asp	Asp	Lys	
	Asp 385	Lys	Ile	Lys	Asp	Lys 390	Ile	Ala	Lys	Asp	Glu 395	Glu	Lys	Lys	Glu	Ser 400	
25	Glu	Leu	Lys	Val	Asp 405	Gly	Glu	Lys	Lys	Asp 410	Ser	Asn	Leu	Ser	Ser 415	Pro	
	Ala	Arg	Asp	Ile 420	Leu	Pro	Leu	Pro	Pro 425	Lys	Thr	Ala	Leu	Asp 430	Leu	Lys	
30	Leu	Glu	Ile 435	Gln	Lys	Val	Lys	Glu 440	Ser	Arg	Asp	Ala	Ile 445	Lys	Leu	Asp	
35	Asn	Leu 450	Gln	Leu	Ala	Lėu	Pro 455	Ser	Val	Cys	Met	Tyr 460	Thr	Phe	Gln	Asn	
	Thr 465	Asn	Lys	Asp	Met	Ser 470	Суз	Leu	Asp	Phe	Ser 475	Asp	Asp	Cys	Arg	Ile 480	
40	Ala	Ala	Ala	Gly	Phe 485	Gln	Asp	Ser	Tyr	Ile 490	Lys	Ile	Trp	Ser	Leu 495	Asp	
	Gly	Ser	Ser	Leu 500	Asn	Asn	Pro	Asn	Ile 505	Ala	Leu	Asn	Asn	Asn 510	Asp	Lys	
45	Asp	Glu	Asp 515	Pro	Thr	Cys	Lys	Thr 520	Leu	Val	Gly	His	Ser 525	Gly	Thr	Val	

- 165 -

	Tyr	Ser 530	Thr	Ser	Phe	Ser	Pro 535	Asp	Asn	Lys	Tyr	Leu 540	Leu	Ser	Gly	Ser
5	Glu 545	Asp	Lys	Thr	Val	Arg 550	Leu	Trp	Ser	Met	Asp 555	Thr	His	Thr	Ala	Leu 560
	Val	Ser	Tyr	Lys	Gly 565	His	Asn	His	Pro	Val 570	Trp	Asp	Val	Ser	Phe 575	Ser
10	Pro	Leu	Gly	His 580	Tyr	Phe	Ala	Thr	Ala 585	Ser	His	Asp	Gln	Thr 590	Ala	Arg
15	Leu	Trp	Ser 595	Cys	Asp	His	·Ile	Tyr 600	Pro	Leu	Arg	Ile	Phe 605	Ala	Gly	His
	Leu	Asn 610	Asp	Val	Asp	Cys	Val 615	Ser	Phe	His	Pro	Asn 620	Gly	Cys	Tyr	Val
20	Phe 625	Thr	Gly	Ser	Ser	Asp 630	Lys	Thr	Cys	Arg	Met 635	Trp	Asp	Val	Ser	Thr 640
	Gly	Asp	Ser	Val	Arg 645	Leu	Phe	Leu	Gly	His 650	Thr	Ala	Pro	Val	Ile 655	Ser
25	Ile	Ala	Val	Cys 660	Pro	Asp	Gly	Arg	Trp 665	Leu	Ser	Thr	Gly	Ser 670	Glu	Asp
30	Gly	Ile	Ile 675	Asn	Val	Trp	Asp	Ile 680	Gly	Thr	Gly	Lys	Arg 685	Leu	Lys	Gln
	Met	Arg 690	Gly	His	Gly	Lys	Asn 695	Ala	Ile	Tyr	Ser	Leu 700	Ser	Tyr	Ser	Lys
35	Glu 705	Gly	Asn	Val	Leu	Ile 710	Ser	Gly	Gly	Ala	Asp 715	His	Thr	Val	Arg	Val 720
	Trp	Asp	Leu	Lys	Lys 725	Ala	Thr	Thr	Glu	Pro 730	Ser	Ala	Glu	Pro	Asp 735	Glu
40	Pro	Phe	Ile	Gly 740	Tyr	Leu	Gly	Asp	Val 745	Thr	Ala	Ser	Ile	Asn 750	Gln	Asp
4 5	Ile	Lys	Glu 755	Tyr	Gly	Arg	Arg	Arg 760	Thr	Val	Ile	Pro	Thr 765	Ser	Asp	Leu
	Val	Ala	Ser	Phe	Tyr	Thr	Lys	Lys	Thr	Pro	Val	Phe	Lys	Val	Lys	Phe

- 166 -

770 775 780

Ser Arg Ser Asn Leu Ala Leu Ala Gly Gly Ala Phe Arg Pro
785 790 795

5

- (2) INFORMATION FOR SEQ ID NO:65:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 439 amino acids
- 10 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: protein
- 15 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 20 (C) INDIVIDUAL ISOLATE: YCU7, Fig. 48
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:
- Met Val Arg Arg Phe Arg Gly Lys Glu Leu Ala Ala Thr Thr Phe Asn
 1 5 10 15
 - Gly His Arg Asp Tyr Val Met Gly Ala Phe Phe Ser His Asp Gln Glu 20 25 30

30

- Lys Ile Tyr Thr Val Ser Lys Asp Gly Ala Val Phe Val Trp Glu Phe 35 40 45
- Thr Lys Arg Pro Ser Asp Asp Asp Asp Asp Glu Ser Glu Asp Asp Asp 35 55 60
 - Lys Gln Glu Glu Val Asp Ile Ser Lys Tyr Ser Trp Arg Ile Thr Lys 65 70 75 80
- Lys His Phe Phe Tyr Ala Asn Gln Ala Lys Val Lys Cys Val Thr Phe 85 90 95
 - His Pro Ala Thr Arg Leu Leu Ala Val Gly Phe Thr Ser Gly Glu Phe 100 105 110

45

Arg Leu Tyr Asp Leu Pro Asp Phe Thr Leu Ile Gln Gln Leu Ser Met

- 167 -

			115					120			1		125		,	
-	Gly	Gln 130	Asn	Pro	Val	Asn	Thr 135		Ser	Val	Asn	Gln 140	Thr	Gly	Glu	Trp
5	Leu 145	Ala	Phe	Gly	Ser	Ser 150	Lys	Leu	Gly	Gln	Leu 155	Leu	Val	Tyr	Glu	Trp 160
10	Gln	Ser	Glu	Ser	Tyr 165	Ile	Leu	Lys	Gln	Gln 170	Gly	His	Phe	Asp	Ser 175	Thr
	Asn	Ser	Leu	Ala 180	Tyr	Ser	Pro	Asp	Gly 185	Ser	Arg	Val	Val	Thr 190	Ala	Ser
15	Glu	Asp	Gly 195	Lys	Ile	Lys	Val	Trp 200	Asp	Ile	Thr	Ser	Gly 205	Phe	Cys	Leu
20	Ala	Thr 210	Phe	Glu	Glu	His	Thr 215	Ser	Ser	Val	Thr	Ala 220	Val	Gln	Phe	Ala
	Lys 225	Arg	Gly	Gln	Val	Met 230	Phe	Ser	Ser	Ser	Leu 235	Asp	Gly	Thr	Val	Arg 240
25	Ala	Trp	Asp	Leu	Ile 245	Arg	Tyr	Arg	Asn	Phe 250	Arg	Thr	Phe	Thr	Gly 255	Thr
	Glu	Arg	Ile	Gln 260	Phe	Asn	Сув	Leu	Ala 265	Val	Asp	Pro	Ser	Gly 270	Glu	Val
30	Val	Cys	Ala 275	Gly	Ser	Leu	Asp	Asn 280	Phe	Asp	Ile	His	Val 285	Trp	Ser	Val
35	Gln	Thr 290	Gly	Gln	Leu	Leu	Asp 295	Ala	Leu	Ser	Gly	His 300	Glu	Gly	Pro	Val
	Ser 305	Cys	Leu	Ser	Phe	Ser 310	Gln	Glu	Asn	Ser	Val 315	Leu	Ala	Ser	Ala	Ser 320
40	Trp	Asp	Lys	Thr	Ile 325	Arg	Ile	Trp	Ser	Ile 330	Phe	Gly	Arg	Ser	Gln 335	Gln
	Val	Glu	Pro	Ile 340		Val	Tyr	Ser	Asp 345		Leu	Ala	Leu	Ser 350	Met	Arg
45	Pro	Asp	Gly 355	_	Glu	Val	Ala	Val 360		Thr	Leu	Lys	Gly 365	Gln	Ile	Ser

- 168 -

. Ile Phe Asn Ile Glu Asp Ala Lys Gln Val Gly Asn Ile Asp Cys Arg 370 375 380 Lys Asp Ile Ile Ser Gly Arg Phe Asn Gln Asp Arg Phe Thr Ala Lys 385 390 5 395 400 Ile Leu Asn Asp Pro Asn Phe Leu Leu Gln Tyr Ile Thr Val Leu Met 405 410 10 Val Trp Leu Leu Trp Leu Val Val Ile Ile Thr Pro Phe Val Tyr Met 425 420 430 Met Phe Gln Met Lys Ser Cys 435 15 (2) INFORMATION FOR SEQ ID NO:66: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 514 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:66: 35 Met Ser Thr Leu Ile Pro Pro Pro Ser Lys Lys Gln Lys Lys Glu Ala Gln Leu Pro Arg Glu Val Ala Ile Ile Pro Lys Asp Leu Pro Asn Val 25 40 Ser Ile Lys Phe Gln Ala Leu Asp Thr Gly Asp Asn Val Gly Gly Ala 40 Leu Arg Val Pro Gly Ala Ile Ser Glu Lys Gln Leu Glu Glu Leu Leu 45 55

60

- 169 -

		Asn 65	Gln	Leu	Asn	Gly	Thr 70	Ser	Asp	Asp	Pro	Val 75	Pro	Tyr	Thr	Phe	Ser 80
	5	Cys	Thr	Ile	Gln	Gly 85	Lys	Lys	Ala	Ser	Asp 90	Pro	Val	Lys	Thr	Ile 95	Asp
		Ile	Thr	Asp	Asn 100	Leu	Tyr	Ser	Ser	Leu 105	Ile	Lys	Pro	Gly	Tyr 110	Asn	Ser
-	10	Thr	Glu	Asp 115	Gln	Ile	Thr	Leu	Leu 120	Tyr	Thr	Pro	Arg	Ala 125	Val	Phe	Lys
-	1.5	Val	Lys 130	Pro	Val	Thr	Arg	Ser 135	Ser	Ser	Ala	Ile	Ala 140	Gly	His	Gly	Ser
•	15	Thr 145	Ile	Leu	Cys	Ser	Ala 150	Phe	Ala	Pro	His	Thr 155	Ser	Ser	Arg	Met	Val 160
:	20	Thr	Gly	Ala	Gly	Asp 165	Asn	Thr	Ala	Arg	Ile 170	Trp	Asp	Cys	Asp	Thr 175	Gln
		Thr	Pro	Met	His 180	Thr	Leu	Lys	Gly	His 185	Tyr	Asn	Trp	Val	Leu 190	Cys	Val
:	25	Ser	Trp	Ser 195	Pro	Asp	Gly	Glu	Val 200	Ile	Ala	Thr	Gly	Ser 205	Met	Asp	Asn
	30	Thr	Ile 210	Arg	Leu	Trp	Asp	Pro 215	Lys	Ser	Gly	Gln	Cys 220	Leu	Gly	Asp	Ala
	30	Leu 225	Arg	Gly	His	Ser	Lys 230	Trp	Ile	Thr	Ser	Leu 235	Ser	Trp	Glu	Pro	Ile 240
	35	His	Leú	Val	Lys	Pro 245	Gly	Ser	Lys	Pro	Arg 250	Leu	Ala	Ser	Ser	Ser 255	Lys
		Asp	Gly	Thr	Ile 260	Lys	Ile	Trp	Asp	Thr 265	Val	Ser	Arg	Val	Cys 270	Gln	Tyr
	40	Thr	Met	Ser 275	_	His	Thr	Asn	Ser 280		Ser	Cys	Val	Lys 285	Trp	Gly	Gly
	45	Gln	Gly 290		. Leu	Tyr	Ser	Gly 295		His	Asp	Arg	Thr 300		Arg	Val	Trp
		Asp	Ile	. Asn	Ser	Gln	Gly	Arg	Cys	Ile	. Asn	Ile	Leu	Lys	Ser	His	Ala

- 170 -

His Trp Val Asn His Leu Ser Leu Ser Thr Asp Tyr Ala Leu Arg Ile Gly Ala Phe Asp His Thr Gly Lys Lys Pro Ser Thr Pro Glu Glu Ala Gln Lys Lys Ala Leu Glu Asn Tyr Glu Lys Ile Cys Lys Lys Asn Gly Asn Ser Glu Glu Met Met Val Thr Ala Ser Asp Asp Tyr Thr Met Phe Leu Trp Asn Pro Leu Lys Ser Thr Lys Pro Ile Ala Arg Met Thr Gly His Gln Lys Leu Val Asn His Val Ala Phe Ser Pro Asp Gly Arg Tyr Ile Val Ser Ala Ser Phe Asp Asn Ser Ile Lys Leu Trp Asp Gly Arg Asp Gly Lys Phe Ile Ser Thr Phe Arg Gly His Ile Ala Ser Val Tyr Gln Val Ala Trp Ser Ser Asp Cys Arg Leu Leu Val Ser Cys Ser Lys Asp Thr Thr Leu Lys Val Trp Asp Val Arg Thr Arg Lys Leu Ser Val Asp Leu Pro Gly Ile Lys Thr Lys Leu Tyr Val Asp Trp Ser Val Asp Gly Lys Arg Val Cys Ser Gly Gly Lys Asp Lys Met Val Arg Leu Trp Thr His

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 852 amino acids

(B) TYPE: amino acid

- 171 -

(D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YKL525, Fig. 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:67: Met Phe Lys Ser Lys Thr Ser Thr Leu Ser Tyr Asp Glu Thr Pro Asn Ser Asn Glu Gly Asp Arg Asn Ala Thr Pro Val Asn Pro Lys Glu Lys Ser Gln Thr Lys His Leu Asn Ile Pro Gly Asp Arg Ser Arg His Ser Ser Ile Ala Asp Ser Lys Arg Ser Ser Ser Arg Tyr Asp Gly Gly Tyr Ser Ala Asp Ile Ile Pro Ala Gln Leu Arg Phe Ile Asp Asn Ile Asp Tyr Gly Thr Arg Leu Arg Lys Thr Leu His Arg Asn Ser Val Val Ser Asn Gly Tyr Asn Lys Leu Ser Glu Asn Asp Arg Trp Tyr Phe Asp Leu Phe Asp Arg Lys Tyr Phe Glu Asn Tyr Leu Glu Glu Pro Thr Tyr Ile Lys Ile Phe Lys Lys Glu Gly Leu Glu Gln Phe Asp Arg Met Phe Leu Ala Gln Glu Leu Lys Ile Pro Asp Val Tyr Lys Ser Thr Thr Tyr

Gln Gly Glu Pro Ala Val Ala Asn Ser Glu Leu Phe Lys Asn Ser Ile

- 172 -

		Cys	Cys	Cys	Thr 180	Phe	Ser	His	Asp	Gly 185	Lys	Tyr	Met	Val	Ile 190	Gly	Cys
	5	Lys	Asp	Gly 195	Ser	Leu	His	Leu	Trp 200	Lys	Val	Ile	Asn	Ser 205	Pro	Val	Lys
		Arg	Ser 210	Glu	Met	Gly	Arg	Ser 215	Glu	Lys	Ser	Val	Ser 220	Ala	Ser	Arg	Ala
:	LO	Asn 225	Ser	Leu	Lys	Ile	Gln 230	Arg	His	Leu	Ala	Ser 235	Ile	Ser	Ser	His	Asn 240
1	L5	Gly	Ser	Ile	Ser	Ser 245	Asn	Asp	Leu	Lys	Pro 250	Ser	Asp	Gln	Phe	Glu 255	Gly
		Pro	Ser	Lys	Gln 260	Leu	His	Leu	Tyr	Ala 265	Pro	Val	Phe	Tyr	Ser 270	Asp	Val
2	20	Phe	Arg	Val 275	Phe	Met	Glu	His	Ala 280	Leu	Asp	Ile	Leu	Asp 285	Ala	Asn	Trp
		Ser	Lys 290	Asn	Gly	Phe	Leu	Ile 295	Thr	Ala	Ser	Met	Asp 300	Lys	Thr	Ala	Lys
2	!5	Leu 305	Trp	His	Pro	Glu	Arg 310	Lys	Tyr	Ser	Leu	Lys 315	Thr	Phe	Val	His	Pro 320
3	0	Asp	Phe	Val	Thr	Ser 325	Ala	Ile	Phe	Phe	Pro 330	Asn	Asp	Asp	Arg	Phe 335	Ile
		Ile	Thr	Gly	Cys 340	Leu	Asp	His	Arg	Cys 345	Arg	Leu	Trp	Ser	Ile 350	Leu	Asp
3	5	Asn	Glu	Val 355	Ser	Tyr	Ala	Phe	Asp 360	Cys	Lys	Asp	Leu	Ile 365	Thr	Ser	Leu
		Thr	Leu 370	Ser	Pro	Pro	Gly	Gly 375	Glu	Tyr	Thr	Ile	Ile 380	Gly	Thr	Phe	Asn
4	0	Gly 385	Tyr	Ile	Tyr	Val	Leu 390	Leu	Thr	His	Gly	Leu 395	Lys	Phe	Val	Ser	Ser 400
4	.5	Phe	His	Val	Ser	Asp 405	Lys	Ser	Thr	Gln	Gly 410	Thr	Thr	Lys	Asn	Ser 415	Phe
		His	Pro	Ser	Ser	Glu	Tyr	Gly	Lys	Val	Gln	His	Gly	Pro	Arg	Ile	Thr

- 173 -

				420					425				•	430		
5	Gly	Leu	Gln 435	Cys	Phe	Phe	Ser	Lys 440	Val	Asp	Lys	Asn	Leu 445	Arg	Leu	Ile
5	Val	Thr 450	Thr	Asn	Asp	Ser	Lys 455	Ile	Gln	Ile	Phe	Asp 460	Leu	Asn	Glu	Lys
10	Lys 465	Pro	Leu	Glu	Leu	Phe 470	Lys	Gly	Phe	Gln	Ser 475	Gly	Ser	Ser	Arg	His
	Arg	Gly	Gln	Phe	Leu 485	Met	Met	Lys	Asn	Glu 490	Pro	Val	Val	Phe	Thr 495	Gly
15	Ser	Asp	Asp	His 500	Trp	Phe	Tyr	Thr	Trp 505	Lys	Met	Gln	Ser	Phe 510	Asn	Lev
20	Ser	Ala	Glu 515	Met	Asn	Cys	Thr	Ala 520	Pro	His	Arg	Lys	Lys 525	Arg	Leu	Ser
	Gly	Ser 530	Met	Ser	Leu	Lys	Gly 535	Leu	Leu	Arg	Ile	Val 540	Ser	Asn	Lys	Ser
25	Thr 545	Asn	Asp	Glu	Cys	Leu 550	Thr	Glu	Thr	Ser	Asn 555	Gln	Ser	Ser	Ser	His
	Thr	Phe	Thr	Asn	Ser 565	Ser	Lys	Asn	Val	Leu 570	Gln	Thr	Gln	Thr	Val 575	Gly
30	Ser	Gln	Ala	Ile 580	Lys	Asn	Asn	His	Tyr 585	Ile	Ser	Phe	His	Ala 590	His	Asr
35	Ser	Pro	Val 595	Thr	Cys	Ala	Ser	Ile 600	Ala	Pro	Asp	Val	Ala 605	Ile	Lys	Asr
	Leu	Ser 610	Leu	Ser	Asn	Asp	Leu 615	Ile	Phe	Glu	Leu	Thr 620	Ser	Gln	Tyr	Phe
40	Lys 625	Glu	Met	Gly	Gln	Asn 630	Tyr	Ser	Glu	Ser	Lys 635	Glu	Thr	Cys	Asp	Asr 640
	Lys	Pro	Asn	His	Pro 645	Val	Thr	Glu	Thr	Gly 650	Gly	Phe	Ser	Ser	Asn 655	Let
45	Ser	Asn	Val					Gly			Leu	Ile	Thr	Thr		Se

- 174 -

Gln Gly Leu Ile Arg Val Phe Arg Thr Asp Ile Leu Pro Glu Ile Arg Lys Lys Ile Ile Glu Lys Phe His Glu Tyr Asn Leu Phe His Leu Glu Ala Ala Gly Lys Ile Asn Asn His Asn Asn Asp Ser Ile Leu Glu Asn Arg Met Asp Glu Arg Ser Ser Thr Glu Asp Asn Glu Phe Ser Thr Thr Pro Pro Ser Asn Thr His Asn Ser Arg Pro Ser His Asp Phe Cys Glu Leu His Pro Asn Asn Ser Pro Val Ile Ser Gly Met Pro Ser Arg Ala Ser Ala Ile Phe Lys Asn Ser Ile Phe Asn Lys Ser Asn Gly Ser Phe Ile Ser Leu Lys Ser Arg Ser Glu Ser Thr Ser Ser Thr Val Phe Gly Pro His Asp Ile Pro Arg Val Ser Thr Thr Tyr Pro Lys Leu Lys Cys Asp Val Cys Asn Gly Ser Asn Phe Glu Cys Ala Ser Lys Asn Pro Ile Ala Gly Gly Asp Ser Gly Phe Thr Cys Ala Asp Cys Gly Thr Ile Leu Asn Asn Phe Arg (2) INFORMATION FOR SEQ ID NO:68: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 798 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

- 175 -

	(iv)	ANTI	-SEN	SE:	NO											
5	(vi)		INI				LATE :	: yri	14 :	10 ye	east,	Fic	g. 5:	L		
	(xi)	SEQU	JENCE	E DES	CRIE	PTION	N: SI	EQ II	ONO:	:68:						
10	Met 1	Ser	Gln	Lys	Gln 5	Ser	Thr	Asn	Gln	Asn 10	Gln	Asn	Gly	Thr	His 15	Glr
	Pro	Gln	Pro	Val 20	Lys	Asn	Gln	Arg	Thr 25	Asn	Asn	Ala	Ala	Gly 30	Ala	Ası
15	Ser	Gly	Gln 35	Gln	Pro	Gln	Gln	Gln 40	Ser	Gln	Gly	Gln	Ser 45	Gln	Gln	Glr
20	Gly	Arg 50	Ser	Asn	Gly	Pro	Phe 55	Ser	Ala	Ser	Asp	Leu 60	Asn	Arg	Ile	Va]
	Leu 65	Glu	Tyr	Leu	Asn	Lys 70	Lys	Gly	Tyr	His	Arg 75	Thr	Glu	Ala	Met	Let 80
25	Arg	Ala	Glu	Ser	Gly 85	Arg	Thr	Leu	Thr	Pro 90	Gln	Asn	Lys	Gln	Ser 95	Pro
	Ala	Asn	Thr	Lys 100	Thr	Gly	Lys	Phe	Pro 105	Glu	Gln	Ser	Ser	Ile 110	Pro	Pro
30	Asn	Pro	Gly 115	Lys	Thr	Ala	Lys	Pro 120	Ile	Ser	Asn	Pro	Thr 125	Asn	Leu	Ser
35	Ser	Lys 130	Arg	Asp	Ala	Glu	Gly 135	Gly	Ile	Val	Ser	Ser 140	Gly	Arg	Leu	Glu
	Gly 145	Leu	Asn	Ala	Pro	Glu 150	Asn	Tyr	Ile	Arg	Ala 155	Tyr	Ser	Met	Leu	Lys 160
40	Asn	Trp	Val	Asp	Ser 165	Ser	Leu	Glu	Ile	Tyr 170	Lys	Pro	Glu	Leu	Ser 175	Туз
	Ile	Met	Tyr	Pro 180	Ile	Phe	Ile	Tyr	Leu 185	Phe	Leu	Asn	Leu	Val 190	Ala	Lys
45	Asn	Pro	Val	_	Ala	Arg	Arg	Phe		Asp	Arg	Phe	Ser		Asp	Phe

- 176 -

	Lys	Asp 210	Phe	His	Gly	Ser	Glu 215	Ile	Asn	Arg	Leu	Phe 220	Ser	Val	Asn	Ser
5	Ile 225	Asp	His	Ile	Lys	Glu 230	Asn	Glu	Val	Ala	Ser 235	Ala	Phe	Gln	Ser	His 240
	Lys	Tyr	Arg	Ile	Thr 245	Met	Ser	Lys	Thr	Thr 250	Leu	Asn	Leu	Leu	Leu 255	Tyr
10	Phe	Leu	Asn	Glu 260	Asn	Glu	Ser	Ile	Gly 265	Gly	Ser	Leu	Ile	Ile 270	Ser	Val
15	Ile	Asn	Gln 275	His	Leu	Asp	Pro	Asn 280	Ile	Val	Glu	Ser	Val 285	Thr	Ala	Arg
15	Glu	Lys 290	Leu	Ala	Asp	Gly	Ile 295	Lys	Val	Leu _.	Ser	Asp 300	Ser	Glu	Asn	Gly
20	Asn 305	Gly	Lys	Gln	Asn	Leu 310	Glu	Met	Asn	Ser	Val 315	Pro	Val	Lys	Leu	Gly 320
	Pro	Phe	Pro	Lys	Asp 325	Glu	Glu	Phe	Val	Lys 330	Glu	Ile	Glu	Thr	Glu 335	Leu
25	Lys	Ile	Lys	Asp 340	Asp	Gln	Glu	Lys	Gln 345	Leu	Asn	Gln	Gln	Thr 350	Ala	Gly
30	Asp	Asn	Tyr 355	Ser	Gly	Ala	Asn	Asn 360	Arg	Thr	Leu	Leu	Gln 365	Glu	Tyr	Lys
	Ala	Met 370	Asn	Asn	Glu	Lys	Phe 375	Lys	Asp	Asn	Thr	Gly 380	Asp	Asp	Asp	Lys
35	Asp 385	Lys	Ile	Lys	Asp	Lys 390	Ile	Āla	Lys	Asp	Glu 395	Glu	Lys	Lys	Glu	Ser 400
	Glu	Leu	Lys	Val	Asp 405	Gly	Glu	Lys	Lys	Asp 410	Ser	Asn	Leu	Ser	Ser 415	Pro
40	Ala	Arg	Asp	Ile 420	Leú	Pro	Leu	Pro	Pro 425	Lys	Thr	Ala	Leu	Asp 430	Leu	Lys
45	Leu	Glu •	Ile 435	Gln	Lys	Val	Lys	Glu 440	Ser	Arg	Asp	Ala	Ile 445	Lys	Leu	Asp
	Asn	Leu	Gln	Leu	Ala	Leu	Pro	Ser	Val	Cys	Met	Tyr	Thr	Phe	Gln	Asn

- 177 -

•		450					455					460				
5	Thr 465	Asn	Lys	Asp	Met	Ser 470	Cys	Leu	Asp	Phe	Ser 475	Asp	Asp	Cys	Arg	Ile 480
•	Ala	Ala	Ala	Gly	Phe 485	Gln	Asp	Ser	Tyr	Ile 490	Lys	Ile	Trp	Ser	Leu 495	Asp
10	Gly	Ser	Ser	Leu 500	Asn	Asn	Pro	Asn	Ile 505	Ala	Leu	Asn	Asn	Asn 510	Asp	Lys
	Asp	Glu	Asp 515	Pro	Thr	Cys	Lys	Thr 520	Leu	Val	Gly	His	Ser 525	Gly	Thr	Val
15	Tyr	Ser 530	Thr	Ser	Phe	Ser	Pro 535	Asp	Asn	Lys	Tyr	Leu 540	Leu	Ser	Ġly	Ser
20	Glu 54 5	Asp	Lys	Thr	Val	Arg 550	Leu	Trp	Ser	Met	Asp 555	Thr	His	Thr	Ala	Leu 560
	Val	Ser	Tyr	Lys	Gly 565	His	Asn	His	Pro	Val 570	Trp	Asp	Val	Ser	Phe 575	Ser
25	Pro	Leu	Gly	His 580	Tyr	Phe	Ala	Thr	Ala 585	Ser	His	Asp	Gln	Thr 590	Ala	Arg
	Leu	Trp	Ser 595	Cys	Asp	His	Ile	Tyr 600	Pro	Leu	Arg	Ile	Phe 605	Ala	Gly	His
30	Leu	Asn 610	Asp	Val	Asp	Cys	Val 615	Ser	Phe	His	Pro	Asn 620	Gly	Cys	Tyr	Val
35	Phe 625	Thr	Gly	Ser	Ser	Asp 630	Lys	Thr	Cys	Arg	Met 635	Trp	Asp	Val	Ser	Thr 640
	Gly	Asp	Ser	Val	Arg 645	Leu	Phe	Leu	Gly	His 650	Thr	Ala	Pro	Val	Ile 655	Ser
40	Ile	Ala	Val	Cys 660	Pro	Asp	Gly	Arg	Trp 665	Leu	Ser	Thr	Gly	Ser 670	Glu	Asp
	Gly	Ile	Ile 675	Asn	Val	Trp	Asp	Ile 680	Gly	Thr	Gly	Lys	Arg 685	Leu	Lys	Gln
45	Met	Arg 690	Gly	His	Gly	Lys	Asn 695	Ala	Ile	Tyr	Ser	Leu 700	Ser	Tyr	Ser	Lys

- 178 -

Glu Gly Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val 705 710 715 Trp Asp Leu Lys Lys Ala Thr Thr Glu Pro Ser Ala Glu Pro Asp Glu 5 725 730 Pro Phe Ile Gly Tyr Leu Gly Asp Val Thr Ala Ser Ile Asn Gln Asp 740 745 10 Ile Lys Glu Tyr Gly Arg Arg Thr Val Ile Pro Thr Ser Asp Leu 755 760 Val Ala Ser Phe Tyr Thr Lys Lys Thr Pro Val Phe Lys Val Lys Phe 770 775 780 15 Ser Arg Ser Asn Leu Ala Leu Ala Gly Gly Ala Phe Arg Pro 785 790 795 20 (2) INFORMATION FOR SEQ ID NO:69: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid 25 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rI, Fig. 1C 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69: Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 40 1 5 10 15 Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 25 30 45

(2) INFORMATION FOR SEQ ID NO:70:

- 179 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rII, Fig. 1C 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70: Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 20 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:71: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rIII, Fig. 1C 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:71: Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg 5 10 45 Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn

- 180 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:72:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: RACK1 protein rIV, Fig. 1C

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 1 5 10 15

Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp
20 25 30

Asn

30

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

40 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

45 (C) INDIVIDUAL ISOLATE: RACK1 protein rV, Fig. 1C

- 181 -(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73: Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser 5 5 Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:74: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rVI, Fig. 1C 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74: Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys Phe Ser Pro Asn Arg 5 10 30 Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile Lys Ile Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:75: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 40 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

45

(iv) ANTI-SENSE: NO

- 182 -

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: RACK1 protein rVII, Fig. 1C

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser Leu Ala Trp Ser Ala Asp

1 5 10 15

10 Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp Asn Leu Val Arg Val Trp
20 25 30

Gln

15

- (2) INFORMATION FOR SEQ ID NO:76:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
- 20 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 25 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 30 (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rI, Fig. 11
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
- Gly His Thr Asp Ala Val Leu Asp Leu Ser Trp Asn Lys Leu Ile Arg

 1 5 10 15

Asn Val Leu Ala Ser Ala Ser Ala Asp Asn Thr Val Ile Leu Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:77:
 - (i) SEQUENCE CHARACTERISTICS:
- 45 (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid

- 183 -

(D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 5 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 10 (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rII, Fig. 11 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:77: Ala His Asn Asp Glu Ile Ser Gly Leu Asp Leu Ser Ser Gln Ile Lys 15 1 5 10 Gly Cys Leu Val Thr Ala Ser Ala Asp Lys Tyr Val Lys Ile Trp Asp 20 25 20 (2) INFORMATION FOR SEQ ID NO:78: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 37 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rIII, Fig. 11 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78: 40 Val His Ser Arg Asp Met Lys Met Gly Val Leu Phe Cys Ser Ser Cys 1 5 10 Cys Pro Asp Leu Pro Phe Ile Tyr Ala Phe Gly Gly Gln Lys Glu Gly

- 184 -

Leu Arg Val Trp Asp 35

45

(2) INFORMATION FOR SEQ ID NO:79: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 10 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 15 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: AAC-RICH protein rI, Fig. 12 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79: Gly Asn Lys Lys Lys Ser Thr Ser Val Ala Trp Asn Ala Asn Gly Thr 10 25 Lys Ile Ala Ser Ser Gly Ser Asp Gly Ile Val Arg Val Trp Asn 30 25 20 (2) INFORMATION FOR SEQ ID NO:80: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 35 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 40 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: AAC-RICH protein rII, Fig. 12

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

- 185 -

Gly His Asp Gly Ser Ile Glu Lys Ile Ser Trp Ser Pro Lys Asn Asn 10 Asp Leu Leu Ala Ser Ala Gly Thr Asp Lys Val Ile Lys Ile Trp Asp 20 25 5 (2) INFORMATION FOR SEQ ID NO:81: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: AAC-RICH protein rIII, Fig. 12 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81: Asp His Leu Ala Leu Ile Asp Leu Pro Thr Ile Lys Thr Leu Lys Ile 15 5 Tyr Lys Phe Asn Gly Glu Glu Leu Asn Gln Val Gly Trp Asp 30 25 30 20 (2) INFORMATION FOR SEQ ID NO:82: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- 186 -

(C) INDIVIDUAL ISOLATE: AAC-RICH protein rIV, Fig. 12

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

5

Gly His Thr Ala Ser Ile Tyr Cys Met Glu Phe Asp Pro Thr Gly Lys

1 10 15

Tyr Leu Ala Ala Gly Ser Ala Asp Ser Ile Val Ser Leu Trp Asp

20 25 30

- (2) INFORMATION FOR SEQ ID NO:83:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

20

15

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BETA TRCP rI, Fig. 13
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

30

Ile His Cys Arg Ser Glu Thr Ser Lys Gly Val Tyr Cys Leu Gln Tyr

1 5 10 15

Asp Asp Gln Lys Ile Val Ser Gly Leu Arg Asp Asn Thr Ile Lys Ile 35 20 25 30

Trp Asp

- 40 (2) INFORMATION FOR SEQ ID NO:84:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

- 187 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 5 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rII, Fig. 13 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84: Gly His Thr Gly Ser Val Leu Cys Leu Gln Tyr Asp Glu Arg Val Ile 5 10 15 Ile Thr Gly Ser Asp Ser Thr Val Arg Val Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:85: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rIII, Fig. 13 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:85: Ile His His Cys Glu Ala Val Leu His Leu Arg Phe Asn Asn Gly Met 5 10 40 Met Val Thr Cys Ser Lys Asp Arg Ser Ile Ala Val Trp Asp

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:

- 188 -

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

5 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

10

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BETA TRCP rIV, Fig. 13
- 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

Gly His Arg Ala Ala Val Asn Val Val Asp Phe Asp Asp Lys Tyr Ile

1 5 10 15

20 Val Ser Ala Ser Gly Asp Arg Thr Ile Lys Val Trp Asn 20 25

- (2) INFORMATION FOR SEQ II: NO:87:
- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 30 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

35

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: BETA TRCP rV, Fig. 13
- 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

Gly His Lys Arg Gly Ile Ala Cys Leu Gln Tyr Arg Asp Arg Leu Val 1 5 10 15

Val Ser Gly Ser Ser Asp Asn Thr Ile Arg Leu Trp Asp
20 25

- 189 -

	(2) INFORMATION FOR SEQ ID NO:88:
5	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 29 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown
	(ii) MOLECULE TYPE: peptide
10	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
15	(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rVI, Fig. 13
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:
20	Gly His Glu Glu Leu Val Arg Cys Ile Arg Phe Asp Asn Lys Arg Ile 1 5 10 15
	Val Ser Gly Ala Tyr Asp Gly Lys Ile Lys Val Trp Asp 20 25
25	(2) INFORMATION FOR SEQ ID NO:89:
30	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown
	(ii) MOLECULE TYPE: peptide
35	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
40	<pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rVII, Fig. 13</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:
45	Glu His Ser Gly Arg Val Phe Arg Leu Gln Phe Asp Glu Phe Gln Ile

10

15

- 190 -

Val Ser Ser His Asp Asp Thr Ile Leu Ile Trp Asp
20 25

(2) INFORMATION FOR SEQ ID NO:90:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rI, Fig. 14

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Ala His Ser Asp Tyr Ile Arg Cys Ile Ala Val His Pro Thr Gln Pro 1 5 10 15

25

Phe Ile Leu Thr Ser Ser Asp Asp Met Leu Ile Lys Leu Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:91:

30

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rII, Fig. 14

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

- 191 -

Gly His Thr His Tyr Val Met Gln Ile Val Ile Asn Pro Lys Asp Asn
1 5 10 15

Asn Gln Phe Ala Ser Ala Ser Leu Asp Arg Thr Ile Lys Val Trp Gln 20 25 30

- (2) INFORMATION FOR SEQ ID NO:92:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rIII, Fig. 14
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

Gly His Glu Lys Gly Val Asn Cys Ile Asp Tyr Tyr Ser Gly Gly Asp 1 5 10 15

Lys Pro Tyr Leu Ile Ser Gly Ala Asp Asp Arg Leu Val Lys Ile Trp
20 25 30

Asp

35 .

- (2) INFORMATION FOR SEQ ID NO:93:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 40 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 45 (iii) HYPOTHETICAL: NO

- 192 -

(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: beta-prime-cop rIV, Fig. 14 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:93: Gly His Ala Gln Asn Val Ser Cys Ala Ser Phe His Pro Glu Leu Pro 10 10 Ile Ile Ile Thr Gly Ser Glu Asp Gly Thr Val Arg Ile Trp His 20 25 (2) INFORMATION FOR SEQ ID NO:94: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rI, Fig. 15 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94: Gly His Met Thr Ser Val Ile Thr Cys Leu Gln Phe Glu Asp Asn Tyr 1 5 10 15 35 Val Ile Thr Gly Ala Asp Asp Lys Met Ile Arg Val Tyr Asp 20 25 30 (2) INFORMATION FOR SEQ ID NO:95: 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown

45

(ii) MOLECULE TYPE: peptide

- 193 -(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rII, Fig. 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95: 10 Gly His Asp Gly Gly Val Trp Ala Leu Lys Tyr Ala His Gly Gly Ile 10 Leu Val Ser Gly Ser Thr Asp Arg Thr Val Arg Val Trp Asp 20 25 15 (2) INFORMATION FOR SEQ ID NO:96: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rIII, Fig. 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96: 35 Gly His Asn Ser Thr Val Arg Cys Leu Asp Ile Val Glu Tyr Lys Asn 1 5 15 Ile Lys Tyr Ile Val Thr Gly Ser Arg Asp Asn Thr Leu His Val Trp 40 20 25

Lys

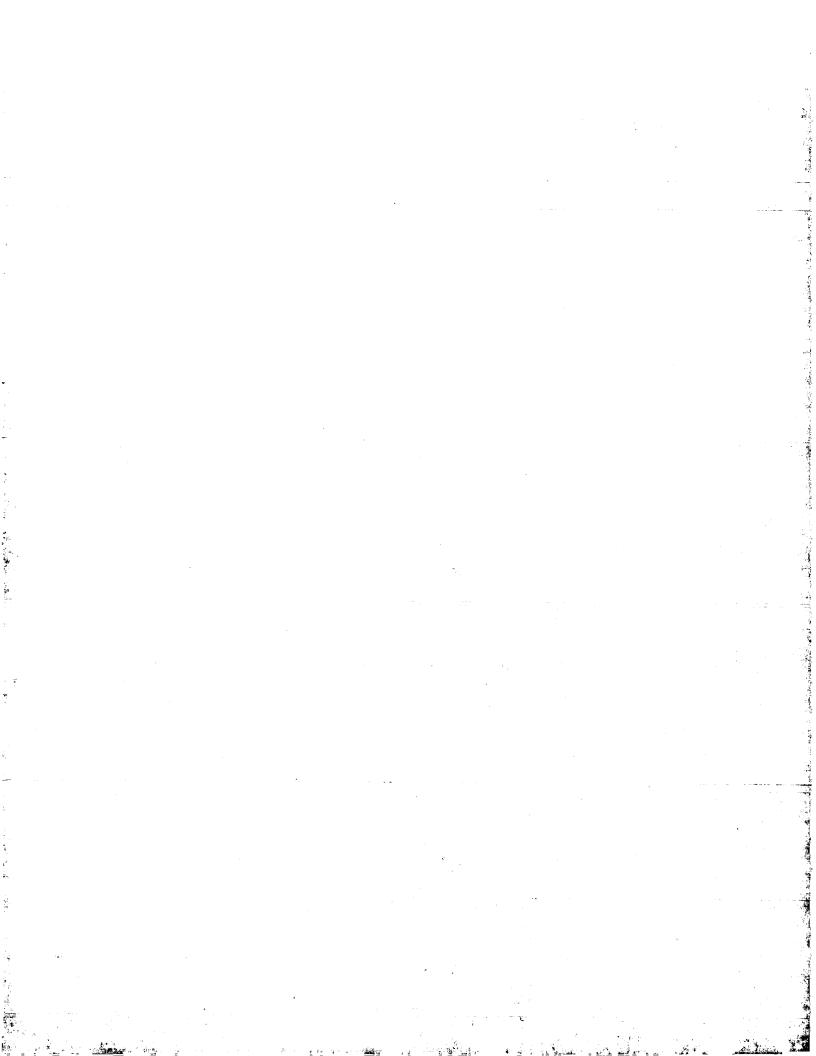
45 (2) INFORMATION FOR SEQ ID NO:97:

WO 95/21252

- 194 -

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(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 29 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
 5
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rIV, Fig. 15
15
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:
          Gly His Met Ala Ser Val Arg Thr Val Ser Gly His Gly Asn Ile Val
          1
                          5
                                                                   15
20
          Val Ser Gly Ser Tyr Asp Asn Thr Leu Ile Val Trp Asp
                      20
     (2) INFORMATION FOR SEQ ID NO:98:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 31 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
30
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
35
        (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rV, Fig. 15
40
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:
         Gly His Thr Asp Arg Ile Tyr Ser Thr Ile Tyr Asp His Glu Arg Lys
                                              10
45
```

Arg Cys Ile Ser Ala Ser Met Asp Thr Thr Ile Arg Ile Trp Asp



- 195 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:99:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rVI, Fig. 15

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Gly His Thr Ala Leu Val Gly Leu Leu Arg Leu Ser Asp Lys Phe Leu

1 5 10 15

25 Val Ser Ala Ala Ala Asp Gly Ser Ile Arg Gly Trp Asp 20 25

(2) INFORMATION FOR SEQ ID NO:100:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

35 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

40

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: GBLP-CHLAMIDOMONAS HOMOLOG rI, Fig. 16

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

- 196 -

Gly His Thr Asn Trp Val Thr Ala Ile Ala Thr Pro Leu Asp Pro Ser 5 Ser Asn Thr Leu Leu Ser Ala Ser Arg Asp Lys Ser Val Leu Val Trp 25 Glu (2) INFORMATION FOR SEQ ID NO:101: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rII, Fig. 25 16 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101: 30 Gly His Ser His Phe Val Gln Asp Val Val Ile Ser Ser Asp Gly Gln 15 Phe Cys Leu Thr Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 20 25 35 (2) INFORMATION FOR SEQ ID NO:102: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 197 -

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rIII, Fig.

16

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Val Asp Asn Arg 1 5 10

10

Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 20

- 15 (2) INFORMATION FOR SEQ ID NO:103:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown 20

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rIV, Fig.
- 30 16
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Gly His Thr Glu Trp Val Ser Cys Val Arg Phe Ser Pro Met Thr Thr

35 10

> Asn Pro Ile Ile Val Ser Gly Gly Trp Asp Lys Met Val Lys Val Trp 20 25

40 Asn

- (2) INFORMATION FOR SEQ ID NO:104:
- 45 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids

- 198 -

(B) TYPE: amino acid(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

5

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 10 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rV, Fig.

16

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Gly His His Gly Tyr Val Asn Thr Val Thr Val Ser Pro Asp Gly Ser

1 5 10 15

- Leu Cys Ala Ser Gly Gly Lys Asp Gly Ile Ala Met Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:105:
- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 30 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

35

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rVI, Fig.

16

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Ile His Cys Leu Cys Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala 1 5 10 15

45

Thr Gln Ser Ser Ile Lys Ile Trp Asp Leu Glu Ser Lys Ser Ile Val

- 199 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:106:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rVII, Fig.

16

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:
- Lys Lys Ala Gln Val Pro Tyr Cys Val Ser Leu Ala Trp Ser Ala Asp

 1 5 10 15
 - Gly Ser Thr Leu Tyr Ser Gly Tyr Thr Asp Gly Gln Ile Arg Val Trp
 20 25 30
- 30 Ala
 - (2) INFORMATION FOR SEQ ID NO:107:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

- 200 -

(C) INDIVIDUAL ISOLATE: cop-1 protein rI, Fig. 17

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

5

Met Ser Thr Arg Ser Lys Leu Ser Cys Leu Ser Trp Asn Lys His Glu

1 5 10 15

Lys Asn His Ile Ala Ser Ser Asp Tyr Glu Gly Ile Val Thr Val Trp

20 25 30

Asp

- 15 (2) INFORMATION FOR SEQ ID NO:108:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
- 20 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: cop-1 protein rII, Fig. 17

30

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:
- Glu Lys Arg Ala Trp Ser Val Asp Phe Ser Arg Thr Glu Pro Ser Met

 1 5 10 15

Leu Val Ser Gly Ser Asp Asp Cys Lys Val Lys Val Trp Cys

- 20 25 30
- 40 (2) INFORMATION FOR SEQ ID NO:109:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

- 201 -

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

5 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: cop-1 protein rIII, Fig. 17

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

Gly His Lys Lys Ala Val Ser Tyr Met Lys Phe Leu Ser Asn Asn Glu

1 5 10 15

15

Leu Ala Ser Ala Ser Thr Asp Ser Thr Leu Arg Leu Trp Asp
20 25 30

(2) INFORMATION FOR SEQ ID NO:110:

20

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

25

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 30 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Coronin (p55) rI, Fig. 19

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

Gly His Lys Ser Ala Val Leu Asp Ile Ala Phe His Pro Phe Asn Glu

1 10 15

40

Asn Leu Val Gly Ser Val Ser Glu Asp Cys Asn Ile Cys Ile Trp Gly
20 25 30

45 (2) INFORMATION FOR SEQ ID NO:111:

- 202 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Coronin (p55) rII, Fig. 19 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111: Gly His Lys Arg Lys Val Gly Thr Ile Ser Phe Gly Pro Val Ala Asp 5 15 20 Asn Val Ala Val Thr Ser Ser Gly Asp Phe Leu Val Lys Thr Trp Asp 20 25 30 25 (2) INFORMATION FOR SEQ ID NO:112: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 30 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Coronin (p55) rIII, Fig. 19 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:112: Gly His Ser Asp Met Ile Thr Ser Cys Glu Trp Asn His Asn Gly Ser 45 1 10

- 203 -

Gln Ile Val Thr Thr Cys Lys Asp Lys Lys Ala Arg Val Phe Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:113:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 38 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN rI, Fig. 18

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:
- Arg His Val Phe Ala Ala Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn 1 5 10 15

25

Leu Lys Thr Lys Ser Ala Val Trp Asp Ser Asn Tyr Val Ala Ala Asn 20 25 30

Thr Arg Tyr Ile Trp Asp 35

30

35

- (2) INFORMATION FOR SEQ ID NO:114:
 - (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN rII, Fig. 18

- 204 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114: Gly His Lys Ser Ala Val Leu Asp Ile Ala Phe His Pro Phe Asn Glu 5 Asn Leu Val Gly Ser Val Ser Glu Asp Cys Asn Ile Cys Ile Trp Gly 25 20 10 (2) INFORMATION FOR SEQ ID NO:115: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids 15 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 25 (C) INDIVIDUAL ISOLATE: CORO PROTEIN rIII, Fig. 18 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:115: 30 Gly His Lys Arg Lys Val Gly Thr Ile Ser Phe Gly Pro Val Ala Asp Asn Val Ala Val Thr Ser Ser Gly Asp Phe Leu Val Lys Thr Trp Asp 35 (2) INFORMATION FOR SEQ ID NO:116: (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 45

(iii) HYPOTHETICAL: NO

- 205 -

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN rIV, Fig. 18

5

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:
- Gly His Ser Asp Met Ile Thr Ser Cys Glu His Asn Gly Ser Gln Ile

 10 1 5 10 15

Val Thr Thr Cys Lys Asp Lys Lys Ala Arg Val Phe Asp

- 15 (2) INFORMATION FOR SEQ ID NO:117:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 20 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CSTF 50kDa rI, Fig. 20

30

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:
- Asp His Val Asp Glu Val Thr Cys Leu Ala Phe His Pro Thr Glu Gln 35 1 5 10 15

Ile Leu Ala Ser Gly Ser Arg Asp Tyr Thr Leu Lys Leu Phe Asp
20 25 30

- 40 (2) INFORMATION FOR SEQ ID NO:118:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

- 206 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rII, Fig. 20 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118: Asp His Val Asp Glu Val Thr Cys Leu Ala Phe His Pro Thr Glu Gln 15 Ile Leu Ala Ser Gly Ser Arg Asp Tyr Thr Leu Lys Leu Phe Asp 20 25 20 (2) INFORMATION FOR SEQ ID NO:119: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid 25 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rIII, Fig. 20 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:119: Ala His Asp Gly Ala Glu Val Cys Ser Ala Ile Phe Ser Lys Asn Ser 40 Lys Tyr Ile Leu Ser Ser Gly Lys Asp Ser Val Ala Lys Leu Trp Glu

25 30

(2) INFORMATION FOR SEQ ID NO:120:

45

- 207 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rIV, Fig. 20 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120: Val His Arg Thr Gln Ala Val Phe Asn His Thr Glu Asp Tyr Val Leu 5 20 Leu Pro Asp Glu Arg Thr Ile Ser Leu Cys Cys Trp Asp (2) INFORMATION FOR SEQ ID NO:121: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown . 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rV, Fig. 20 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:121: Gly His Asn Asn Ile Val Arg Cys Ile Val His Ser Pro Thr Asn Pro 10 45 Gly Phe Met Thr Cys Ser Asp Phe Arg Ala Arg Phe Trp Tyr

- 208 -

20 25 30 (2) INFORMATION FOR SEQ ID NO:122: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 10 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 15 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rI, Fig. 23 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:122: 20 Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Asn Asp Ser Arg 5 25 Asn Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Val Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:123: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 35 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rII, Fig. 23

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

(vi) ORIGINAL SOURCE:

- 209 -

Gly His Gly Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln 5 Ile Val Thr Ser Ser Gly Asp Met Ser Cys Gly Leu Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:124: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rIII, Fig. 23 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:124: 25 Gly His Thr Gly Asp Val Met Ala.Leu Ser Leu Ala Pro Gln Cys Lys 10 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp 30 20 25 (2) INFORMATION FOR SEQ ID NO:125: (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rIV, Fig. 23

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(vi) ORIGINAL SOURCE:

- 210 -(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125: Gly His Glu Ser Asp Ile Asn Ala Val Thr Phe Phe Pro Asn Gly Gln 5 10 5 Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 25 30 (2) INFORMATION FOR SEQ ID NO:126: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rV, Fig. 23 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:126: Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Lys 5 30 Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val 20 25 30 Trp Asp 35 (2) INFORMATION FOR SEQ ID NO:127: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 211 -

(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rVI, Fig. 23 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:127: Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Glu Asn Gly Met 10 5 10 Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Arg Val Trp Asn 25 20 (2) INFORMATION FOR SEQ ID NO:128: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rI, Fig. 24 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:128: Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 5 15 35 Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 20 25 30 (2) INFORMATION FOR SEQ ID NO:129: 40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

- 212 -

(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rII, Fig. 24 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 5 10 15 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 25 20 (2) INFORMATION FOR SEQ ID NO:130: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rIII, Fig. 24 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130: Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg 10 40 Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 25 30 20 (2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:

- 213 -(A) LENGTH: 33 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 5 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rIV, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:131: 15 Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 10 1 · Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp 25 20 Asn (2) INFORMATION FOR SEQ ID NO:132: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rV, Fig. 24 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser

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- 214 -

Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp
20 25 30

(2) INFORMATION FOR SEQ ID NO:133:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rVI, Fig. 24

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys

1 5 10 15

25

Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 20 25 30

Lys Ile Trp Asp 35

30

- (2) INFORMATION FOR SEQ ID NO:134:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

40

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rVII, Fig. 24

PCT/US95/01210

- 215 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134: Ala Glu Pro Pro Gln Cys Thr Ser Leu Ala Trp Ser Ala Asp Gly Gln 10 5 5 Thr Leu Phe Ala Gly Tyr Thr Asp Asn Leu Val Arg Val Trp Gln 25 20 (2) INFORMATION FOR SEQ ID NO:135: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rI, Fig. 21 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:135: Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg 30 Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp 25 30 -20

- (2) INFORMATION FOR SEQ ID NO:136: 35
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 amino acids

(B) TYPE: amino acid

40 (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 216 -

Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln

1 10 15

- 10 Ile Val Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:137:
- 15 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid(D) TOPOLOGY: unknown
- 20 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

25

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rIII, Fig. 21
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

Gly His Thr Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Thr Arg 1 5 10 15

- Leu Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:138:
- 40 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 45 (ii) MOLECULE TYPE: peptide

PCT/US95/01210

- 217 -

(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rIV, Fig. 21 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:138: 10 Gly His Glu Ser Asp Ile Asn Ala Ile Cys Phe Phe Pro Asn Gly Asn 10 Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 25 15 (2) INFORMATION FOR SEQ ID NO:139: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rV, Fig. 21 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:139: 35 Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ser Phe Ser Lys 5 10 Ser Gly Arg Leu Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val 40 20 25 30 Trp Asp

(2) INFORMATION FOR SEQ ID NO:140: 45

- 218 -

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(i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 31 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: unknown
 5
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
                (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rVI, Fig. 21
15
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:
          Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met
                          5
                                               10
20
          Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn
                      20
                                          25
                                                               30
     (2) INFORMATION FOR SEQ ID NO:141:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 31 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
30
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rI, Fig. 22
40
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:
         Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg
                                              10
45
         Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp
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- 219 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:142:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rII, Fig. 22

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln

1 10 15

25 Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:143:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

35 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

40

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rIII, Fig. 22

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

- 220 -

Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg 10 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp 5 20 25 (2) INFORMATION FOR SEQ ID NO:144: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 20 (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rIV, Fig. 22 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:144: 25 Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr 1 5 10 15 Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 30 (2) INFORMATION FOR SEQ ID NO:145: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids 35 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rV, Fig. 22

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(vi) ORIGINAL SOURCE:

- 221 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145. Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg 5 10 Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile 20 25 10 Trp Asp (2) INFORMATION FOR SEQ ID NO:146: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO . 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rVI, Fig. 22 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:146: 30 Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn 35 25 (2) INFORMATION FOR SEQ ID NO:147: (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 45

(iii) HYPOTHETICAL: NO

- 222 -(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rI, Fig. 25 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:147: Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg 10 5 10 Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp 20 25 15 (2) INFORMATION FOR SEQ ID NO:148: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rII, Fig. 25 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:148: Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln 35 10 Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp

40 (2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: unknown

- 223 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 5 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rIII, Fig. 25 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:149: Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg 5 10 15 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp 25 20 30 (2) INFORMATION FOR SEQ ID NO:150: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rIV, Fig. 25 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:150: Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr 5 10 15 40 Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:151:

(i) SEQUENCE CHARACTERISTICS:

- 224 -

(A) LENGTH: 34 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rV, Fig. 25 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:151: Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg 10 20 Ser Gly Arg Leu Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile 20 25 Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:152: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 30 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 40 (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rVI, Fig. 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met

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- 225 -

Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn 20 25 30

(2) INFORMATION FOR SEQ ID NO:153:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rI, Fig. 26

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- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:
- Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Tyr Asp Ser Arg

 1 5 10 15

25

- Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp
 20 25 30
- (2) INFORMATION FOR SEQ ID NO:154:

30

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rII, Fig. 26

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

- 226 -

Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Gly Gln 5 10 Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 5 (2) INFORMATION FOR SEQ ID NO:155: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rIII, Fig. 26 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:155: 25 Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ser Pro Asp Leu Lys 10 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ser Lys Leu Trp Asp 30 25 (2) INFORMATION FOR SEQ ID NO:156: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 35 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 45 (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rIV, Fig. 26

- 227 -

	(xi)	SEQUENCE I	ESCRIP	TION: S	EQ II	ONO:	:156	:					
5	Gly 1	His Ile So	er Asp 5	Ile Asn	Ala	Val	Ser 10	Phe	Phe	Pro	Ser	Gly 15	Tyr
	Ala	Phe Ala Ti	_	Ser Asp	Asp	Ala 25	Thr	Cys	Arg	Leu	Phe 30	Asp	
10	(2) INFO	RMATION FO	SEQ I	D NO:15	7:								
	(i)	SEQUENCE (A) LENG(B) TYPE	TH: 34 amino	amino a									
15		(D) TOPO	LOGY: u	nknown									
	(ii)	MOLECULE '	TYPE: p	eptide									
20	(iii)	HYPOTHETI	CAL: NO)									
	(iv)	ANTI-SENS	E: NO										
	(vi)	ORIGINAL (C) INDI			: G-1	3eta4	l (moi	ıse)	rV,	Fig.	. 26		
25		•											
	(xi)	SEQUENCE 1	DESCRIP	TION: S	EQ II	ONO	:157:	:					
30	Ser 1	His Asp A	sn Ile 5	Ile Cys	Gly	Ile	Thr 10	Ser	Val	Ala	Phe	Ser 15	Lys
	_												
	Ser	Gly Arg L		Leu Ala	Gly	Tyr 25	Asp	Asp	Phe	Asn	Cys 30		Val
35	Trp	Asp											
	(2) INFO	RMATION FO	R SEQ I	D NO:15	8:								
40	·(i)	SEQUENCE (A) LENG (B) TYPE (D) TOPO	TH: 31 : amino	amino a									

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(ii) MOLECULE TYPE: peptide

- 228 -

(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rVI, Fig. 26 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:158: 10 Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met 10 Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Arg Ile Trp Asn 25 20 15 (2) INFORMATION FOR SEQ ID NO:159: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 30 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GROUCHO PROT. DRSPH rI, Fig. 27 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:159: 35 Thr Ser Ala Ala Pro Ala Cys Tyr Ala Leu Ala Ser Pro Asp Ser Lys 5 Val Cys Phe Ser Cys Cys Ser Asp Gly Asn Ile Ala Val Trp Asp 40 (2) INFORMATION FOR SEQ ID NO:160:

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid

(A) LENGTH: 31 amino acids

	- 229 -
	(D) TOPOLOGY: unknown
	(ii) MOLECULE TYPE: peptide
5	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
10	(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GROUCHO PROT. DRSPH rII, Fig. 27
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:
15	Gly His Thr Asp Gly Ala Ser Cys Ile Asp Ile Ser Pro Asp Gly Ser 1 5 10 15
	Arg Leu Trp Thr Gly Gly Leu Asp Asn Thr Val Arg Ser Trp Asp
20	(2) INFORMATION FOR SEQ ID NO:161:
25	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown
	(ii) MOLECULE TYPE: peptide
30	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
35	<pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rI, Fig. 28</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:
40	Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Ala Ser Asp Ser Arg 1 5 10 15
	Asn Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Val Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:162:

- 230 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rII, Fig. 28 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:162: Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Ile Asp Asp Asn Gln ı 5 10 15 20 Ile Val Thr Ser Ser Gly Asp Met Thr Cys Ala Leu Trp Asn 20 25 30 (2) INFORMATION FOR SEQ ID NO:163: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rIII, Fig. 28 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:163: Gly His Thr Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Met Arg 5 10 45

Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Phe Asp

- 231 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:164:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: GTP binding prt squid rIV, Fig. 28

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

Gly His Glu Ser Asp Ile Asn Ala Ile Thr Tyr Phe Pro Asn Gly Phe 1 5 10 15

25 Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:165:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

35 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

40

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: GTP binding prt squid rV, Fig. 28

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

- 232 -

Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Lys 5 10 Ser Gly Arg Leu Leu Gly Gly Tyr Asp Asp Phe Asn Cys Asn Val 25 5 Trp Asp (2) INFORMATION FOR SEQ ID NO:166: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rVI, Fig. 28 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:166: Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Glu Asp Gly Met 30 Ala Val Ala Thr Gly Ser Trp Asp 20 (2) INFORMATION FOR SEQ ID NO:167: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 40 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

- 233 -

(vi) ORIGINAL SOURCE:
 (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rI, Fig. 29

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

Gly His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Pro Asn Leu Ser

1 5 10 15

Gly His Leu Leu Ser Ala Ser Asp Asp His Thr Ile Cys Leu Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:168:

15

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

20

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETIC.L: NO
- 25 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rII, Fig. 29

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Gly His Thr Ala Val Val Glu Asp Val Ser Trp His Leu Leu His Glu

1 5 10 15

35

Ser Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp 20 25 30

- 40 (2) INFORMATION FOR SEQ ID NO:169:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: unknown

- 234 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 5 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rIII, Fig. 29 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:169: Ser His Ser Val Asp Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe 5 10 15 Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr 20 25 Val Ala Leu Trp Asp 20 35 (2) INFORMATION FOR SEQ ID NO:170: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 37 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rIV, Fig. 29 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:170: 40 Leu His Ser Phe Glu Ser His Lys Asp Glu Ile Phe Gln Val Gln Trp 5 10 Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr Asp Arg Arg

- 235 -

Leu Asn Val Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:171:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rV, Fig. 29

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:
- Ile Gly Glu Glu Gln Ser Pro Glu Asp Ala Glu Asp Gly Pro Fro Glu

 1 5 10 15

25

Leu Leu Phe Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser 20 25 30

Trp Asn

30

- (2) INFORMATION FOR SEQ ID NO:172:
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

40

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rI, Fig. 30

- 236 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172: Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 5 Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 10 (2) INFORMATION FOR SEQ ID NO:173: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 25 (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rII, Fig. 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:173: 30 Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 1 5 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 20 25 30 35 (2) INFORMATION FOR SEQ ID NO:174: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 40 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

45

(iii) HYPOTHETICAL: NO

- 237 -

(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rIII, Fig. 30 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:174: Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg 10 Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 25 15 (2) INFORMATION FOR SEQ ID NO:175: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rIV, Fig. 30 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:175: Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 35 10 Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp 25 20 40 Asn

(2) INFORMATION FOR SEQ ID NO:176:

45 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

- 238 -

(B) TYPE: amino acid
(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

5

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 10 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rV, Fig. 30
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

15

Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser

1 5 10 15

Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:177:
- (i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 36 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

30

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 35 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rVI, Fig. 30
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

40

Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys

1 5 10 15

Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
45 20 25 30

- 239 -

Lys Ile Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:178:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 38 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rVII, Fig. 30

20 - -

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:
- Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser Leu

 1 5 10 15

25

Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp Asn 20 25 30

Leu Val Arg Val Trp Gln

30

35

- 0 35
 - (2) INFORMATION FOR SEQ ID NO:179:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF-7442-human rI, Fig. 31

- 240 -

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:179:							
	(3.1)	Digolated Discarling. Dig 15 No.173.							
_	_	His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Ser Asn Leu Ser							
5	1	5 10 15							
	Gly	His Leu Leu Ser Ala Ser Asp Asp His Thr Val Cys Leu Trp Asp							
		20 25 30							
10									
	(2) INFO	RMATION FOR SEQ ID NO:180:							
	(i)	SEQUENCE CHARACTERISTICS:							
	(=/	(A) LENGTH: 32 amino acids							
15		(B) TYPE: amino acid							
		(D) TOPOLOGY: unknown							
	(ii)	MOLECULE TYPE: peptide							
20	(iii)	HYPOTHETICAL: NO							
	(iv)	ANTI-SENSE: NO							
	()	ORIGINAL SOURCE:							
25	(VI)	(C) INDIVIDUAL ISOLATE: IEF-7442-human rII, Fig. 31							
	(xi)	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:							
	(222)	begoined beschiffs. Beg is No.100.							
30		His Ser Ala Val Val Glu Asp Val Ala Trp His Leu Leu His Glu							
	. 1	5 10 15							
	Ser	Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp							
35		20 25 30							
	(2) INFO	RMATION FOR SEQ ID NO:181:							
	(i)	SEQUENCE CHARACTERISTICS:							
40		(A) LENGTH: 32 amino acids							
		(B) TYPE: amino acid							
		(D) TOPOLOGY: unknown							
	(ii)	MOLECULE TYPE: peptide							
45									

(iii) HYPOTHETICAL: NO

- 241 -

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: IEF-7442-human rIII, Fig. 31

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe Asn Pro Tyr Ser Glu

10 1 5 10 15

Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr Val Ala Leu Trp Asp
20 25 30

15

20

- (2) INFORMATION FOR SEQ ID NO:182:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- 25 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 30 (C) INDIVIDUAL ISOLATE: IEF-7442-human rIV, Fig. 31
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:
- Val His Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr

 1 5 10 15

Asp Arg Arg Leu Asn Val Trp Asp
20

40

- (2) INFORMATION FOR SEQ ID NO:183:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

45 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

- 242 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF-7442-human rV, Fig. 31 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:183: Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn Glu Pro 15 Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Ile Trp Gln 20 25 30 20 (2) INFORMATION FOR SEQ ID NO:184: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Insulin-like GF binding 35 protein complex rI, Fig. 32 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:184:

Ala His Thr Pro Ala Leu Ala Ser Leu Gly Leu Ser Asn Asn Arg Leu

1 5 10 15

Ser Arg Leu Glu Asp Gly Leu Phe Glu Gly Leu Gly Ser Leu Trp Asp
20 25 30

- 243 -

(2) INFORMATION FOR SEQ ID NO:185: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind. 15 pro. complex-rat rI, Fig. 33 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:185: 20 Thr His Thr Pro Ser Leu Ala Ser Leu Ser Leu Ser Ser Asn Leu Leu 10 Gly Arg Leu Glu Glu Gly Leu Phe Gln Gly Leu Ser His Leu Trp Asp 25 20 25 (2) INFORMATION FOR SEQ ID NO:186: (i) SEQUENCE CHARACTERISTICS: 30 (A) LENGTH: 47 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 40 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind.

pro. complex-rat rII, Fig. 33

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

- 244 -

Asn His Leu Glu Thr Leu Ala Glu Gly Leu Phe Ser Ser Leu Gly Arg 10 Val Arg Tyr Leu Ser Leu Arg Asn Asn Ser Leu Gln Thr Phe Ser Pro 25 20 Gln Pro Gly Leu Glu Arg Leu Trp Leu Asp Ala Asn Pro Trp Asp 40 (2) INFORMATION FOR SEQ ID NO:187: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: LIS1 (human) rI, Fig. 34 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:187: Gly His Arg Ser Pro Val Thr Arg Val Ile Phe His Pro Val Phe Ser 30 Val Met Val Ser Ala Ser Glu Asp Ala Thr Ile Lys Val Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:188: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

(iv) ANTI-SENSE: NO

45

(iii) HYPOTHETICAL: NO

- 245 -

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: LIS1 (human) rII, Fig. 34

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Gly His Thr Asp Ser Val Gln Asp Ile Ser Phe Asp His Ser Gly Lys

1 10 15

- Leu Leu Ala Ser Cys Ser Ala Asp Met Thr Ile Lys Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:189:
- 15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

- 20 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

25

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: LIS1 (human) rIII, Fig. 34
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

Gly His Asp His Asn Val Ser Ser Val Ala Ile Met Pro Asn Gly Asp 1 5 10 15

- His Ile Val Ser Ala Ser Arg Asp Lys Thr Ile Lys Met Trp Glu 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:190:
- 40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

45 (ii) MOLECULE TYPE: peptide

PCT/US95/01210 WO 95/21252

- 246 -

(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 5 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: LIS1 (human) rIV, Fig. 34 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:190: 10 Gly His Arg Glu Trp Val Arg Met Val Arg Pro Asn Gln Asp Gly Thr 10 Leu Ile Ala Ser Cys Ser Asn Asp Gln Thr Val Arg Val Trp Val 25 30 20 15 (2) INFORMATION FOR SEQ ID NO:191: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: LISI (human) rV, Fig. 34 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:191: 35 Gly Ser Glu Thr Lys Lys Ser Gly Lys Pro Gly Pro Phe Leu Leu Ser 1 5 15 10 Gly Ser Arg Asp Lys Thr Lys Met Trp Asp 25 40 20 (2) INFORMATION FOR SEQ ID NO:192:

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids

45

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

5 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

10 (C) INDIVIDUAL ISOLATE: LIS1 (human) rVI, Fig. 34

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

15 Gly His Asp Asn Trp Val Arg Gly Val Leu Phe His Ser Gly Gly Lys
1 5 10 15

Phe Ile Leu Ser Cys Ala Asp Asp Lys Thr Leu Arg Val Trp Asp 20 25 30

20

- (2) INFORMATION FOR SEQ ID NO:193:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

25 (B) TYPE: amino acid

(ii) MOLECULE TYPE: peptide

(D) TOPOLOGY: unknown

- 30 (iii) HYPOTHETICAL: NO
- - (vi) ORIGINAL SOURCE:

(iv) ANTI-SENSE: NO

35 (C) INDIVIDUAL ISOLATE: LIS1 (human) rVII, Fig. 34

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Ala His Glu His Phe Val Thr Ser Leu Asp Phe His Lys Thr Ala Pro 1 5 10 15

Tyr Val Val Thr Gly Ser Val Asp Gln Thr Val Lys Val Trp Glu 20 25 30

45

(2) INFORMATION FOR SEQ ID NO:194:

- 248 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MD6 rI, Fig. 35 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:194: Gly His Ser Ala Arg Val Tyr Ala Leu Tyr Tyr Lys Asp Gly Leu Leu 5 15 20 Cys Thr Gly Ser Asp Asp Leu Ser Ala Lys Leu Trp Asp 20 (2) INFORMATION FOR SEQ ID NO:195: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MD6 rII, Fig. 35 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:195: Thr His Thr Cys Ala Ala Val Lys Phe Asp Glu Gln Lys Leu Val Thr 10 15 45

Gly Ser Phe Asp Asn Thr Val Ala Cys Trp Glu

- 249 -

20 25

(2) INFORMATION FOR SEQ ID NO:196:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: MD6 rIII, Fig. 35

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

Gly His Thr Gly Ala Val Phe Ser Val Asp Tyr Ser Asp Glu Leu Asp 1 5 10 15

25 Ile Leu Val Ser Gly Ser Ala Asp Phe Ala Val Lys Val Trp Ala 20 25 30

(2) INFORMATION FOR SEQ ID NO:197:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

35 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

40

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: MD6 rIV, Fig. 35

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:197:

- 250 -Gly His Thr Glu Trp Val Thr Lys Val Val Leu Gln Lys Cys Lys Val Lys Ser Leu Leu His Ser Pro Gly Asp Tyr Ile Leu Leu Ser Ala Asp 5 Lys Tyr Glu Ile Lys Ile Trp Pro (2) INFORMATION FOR SEQ ID NO:198: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MSL1 rI, Fig. 36 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:198: Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe Asn Tyr Lys Asn Ser 30 10 Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg Leu Asn Leu Trp Asp 20 25 35 (2) INFORMATION FOR SEQ ID NO:199: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 251 -

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: MSL1 rII, Fig. 36

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:199:

Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe Asp

10 1 5 10 15

Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu Trp
20 25 30

15 Asp

- (2) INFORMATION FOR SEQ ID NO:200:
- 20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

- 25 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

30

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: MSL1 rIII, Fig. 36
- 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:200:

Gly His Met Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro 1 5 10 15

Trp Leu Met Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys
20 25 30

(2) INFORMATION FOR SEQ ID NO:201:

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(i) SEQUENCE CHARACTERISTICS:

- 252 -

(A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MUS MUSCULUS PROTEIN rI, Fig. 37 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:201: Gly His Ser Gly Cys Val Asn Thr Val His Phe Asn Gln His Gly Thr 10 Leu Leu Ala Ser Gly Ser Asp Asp Leu Lys Val Ile Val Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:202: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 50 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MUS MUSCULUS PROTEIN rII, Fig. 37 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:202: Gly His Ile Phe Ile Trp Glu Lys Ser Ser Cys Gln Ile Val Gln Phe 1 5 10 15

45 Leu Glu Ala Asp Glu Gly Gly Thr Ile Asn Cys Ile Asp Ser His Pro 20 25 30

- 253 -

Tyr Leu Pro Val Leu Ala Ser Ser Gly Leu Asp His Glu Val Lys Ile 35 40 45

Trp Ser

50

- (2) INFORMATION FOR SEQ ID NO:203:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: ORF RB1 rI, Fig. 38
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:

Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe Asn Tyr Lys Asn Ser 1 5 10 15

- Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg Leu Asn Leu Trp Asp

 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:204:

35

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

- 254 -

(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: ORF RB1 rII, Fig. 38 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:204: Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe Asp 10 10 Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu Trp 20 25 30 Asp 15 (2) INFORMATION FOR SEQ ID NO:205: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: ORF RB1 rIII, Fig. 38 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:205: 35 Gly His Met Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro 1.0 Trp Leu Met Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys 20 25 40 (2) INFORMATION FOR SEQ ID NO:206:

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid

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(A) LENGTH: 37 amino acids

- 255 -

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

5 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

10 (C) INDIVIDUAL ISOLATE: Periodic Trp prt rI, Fig. 39

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:206:

15 Gly His Ile Thr Thr His His Thr Asp Ala Val Leu Ser Met Ala His 1 5 10 15

Asn Lys Tyr Phe Arg Ser Val Leu Ala Ser Thr Ser Ala Asp His Thr
20 25 30

20

Val Lys Leu Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:207:

25

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 47 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

30

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 35 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Periodic Trp prt rII, Fig. 39

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

Ile His Ser Asn Lys Asn Val Ser Ser Glu Trp His Met Leu Asn
1 5 10 15

45

Gly Ser Ile Leu Leu Thr Gly Gly Tyr Asp Ser Arg Val Ala Leu Thr

- 256 -20 25 30 Asp Val Arg Ile Ser Asp Glu Ser Gln Met Ser Lys Tyr Trp Ser 5 (2) INFORMATION FOR SEQ ID NO:208: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid 10 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP rI, Fig. 40 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208: Gly His Lys Asp Thr Val Cys Ser Leu Ser Ser Gly Lys Phe Gly Thr 25 Leu Leu Ser Gly Ser Trp Asp Thr Thr Ala Lys Val Trp Leu 20 25 30 30 (2) INFORMATION FOR SEQ ID NO:209: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 35 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO

(C) INDIVIDUAL ISOLATE: PLAP rII, Fig. 40

(iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

PCT/US95/01210 WO 95/21252

- 257 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:209: Gly His Thr Ala Ala Val Trp Ala Val Lys Ile Leu Pro Glu Gln Gly 5 Leu Met Leu Thr Gly Ser Ala Asp Lys Thr Ile Lys Leu Trp Lys 25 (2) INFORMATION FOR SEQ ID NO:210: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP rIII, Fig. 40 . 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:210: Gly His Glu Asp Cys Val Arg Gly Leu Ala Ile Leu Ser Glu Thr Glu 5 10 30 Phe Leu Ser Cys Ala Asn Asp Ala Ser Ile Arg Arg Trp Gln 20 25 30 (2) INFORMATION FOR SEQ ID NO:211: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 40 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

45

(iv) ANTI-SENSE: NO

- 258 -

(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP rIV, Fig. 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:211: Gly His Thr Asn Tyr Ile Tyr Ser Ile Ser Val Phe Pro Asn Ser Lys 5 Asp Phe Val Thr Thr Ala Glu Asp Arg Ser Leu Arg Ile Trp Lys 10 20 25 (2) INFORMATION FOR SEQ ID NO:212: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -HUMAN. rI, Fig. 41 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:212: Gly His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Pro Asn Leu Ser 5 10 15 35 Gly His Leu Leu Ser Ala Ser Asp Asp His Thr Ile Cys Leu Trp Asp 20 25

40 (2) INFORMATION FOR SEQ ID NO:213:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown 45

- 259 -

(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -HUMAN rII, Fig. 41 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:213: Gly His Thr Ala Val Val Glu Asp Val Ser Trp His Leu Leu His Glu 15 10 Ser Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp 20 25 20 (2) INFORMATION FOR SEQ ID NO:214: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 37 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -35 HUMAN rIII, Fig. 41 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:214: 40 Ser His Ser Val Asp Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe 5 10 Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr

25

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- 260 -

Val Ala Leu Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:215:
5
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

10

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

15 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN - HUMAN rIV, Fig. 41

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:

Ser His Lys Asp Glu Ile Phe Gln Val Gln Trp Ser Pro His Asn Glu

25 1 5 10 15

Thr Ile Leu Ala Ser Ser Gly Thr Asp Arg Arg Leu Asn Val Trp Asp 20 25 30

30

35

(2) INFORMATION FOR SEQ ID NO:216:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

40 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

45 (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN HUMAN rV, Fig. 41

- 261 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216: Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Val Trp Gln 20 25 10 (2) INFORMATION FOR SEQ ID NO:217: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 25 (C) INDIVIDUAL ISOLATE: S253 PROTEIN rI, Fig. 42 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:217: 30 Glu His Ala Leu Asp Ile Leu Asp Ala Asn Trp Ser Lys Asn Gly Phe 5 10 15 Leu Ile Thr Ala Ser Met Asp Lys Thr Ala Lys Leu Trp His 20 25 30 35 (2) INFORMATION FOR SEQ ID NO:218: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids 40 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

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(iii) HYPOTHETICAL: NO

- 262 -

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: S253 PROTEIN rII, Fig. 42

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:218:

Val His Pro Asp Phe Val Thr Ser Ala Ile Phe Phe Pro Asn Asp Asp

10 1 5 10 15

Arg Phe Ile Ile Thr Gly Cys Leu Asp His Arg Cys Arg Leu Trp Ser 20 25 30

15

- (2) INFORMATION FOR SEQ ID NO:219:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

20 (B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 25 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 30 (C) INDIVIDUAL ISOLATE: SOF1 rI, Fig. 43
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:219:
- Gly His Arg Asp Gly Val Tyr Ala Ile Ala Lys Asn Tyr Gly Ser Leu

 1 5 10 15

Asn Lys Leu Ala Thr Gly Ser Ala Asp Gly Val Ile Lys Tyr Trp
20 25 30

40

- (2) INFORMATION FOR SEQ ID NO:220:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35 amino acids

45 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

- 263 -(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: SOF1 rII, Fig. 43 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:220: Gly Leu Cys Val Thr Gln Pro Arg Phe His Asp Lys Lys Pro Asp Leu 10 5 15 Lys Ser Gln Asn Phe Met Leu Ser Cys Ser Asp Asp Lys Thr Val Lys 20 25 Leu Trp Ser 20 35 (2) INFORMATION FOR SEQ ID NO:221: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 35 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: SOF1 rIII, Fig. 43 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:221: 40 Gly Leu Ile Arg Thr Phe Asp Gly Glu Ser Ala Phe Gln Gly Ile Asp

Ser His Arg Glu Asn Ser Thr Phe Ala Thr Gly Gly Ala Lys Ile His

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- 264 -

Leu Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:222:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 39 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

10

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

15 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: SOF1 rIV, Fig. 43

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:222:

Gly His Ser Arg Glu Ile Tyr His Thr Lys Arg Met Gln His Val Phe 1 5 10 15

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Val Lys Tyr Ser Met Asp Ser Lys Tyr Ile Ile Ser Gly Ser Asp Asp 20 25 30

Gly Asn Val Arg Leu Trp Arg

(2) INFORMATION FOR SEQ ID NO:223:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

45 (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: STE4-YEAST rI, Fig. 44

- 265 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223: Gly His Asn Asn Lys Ile Ser Asp Phe Arg Trp Ser Arg Asp Ser Lys 5 10 Arg Ile Leu Ser Ala Ser Gln Asp Gly Phe Met Leu Ile Trp Asp 25 10 (2) INFORMATION FOR SEQ ID NO:224: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: STE4-YEAST rII, Fig. 44 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:224: Gly His Thr Cys Tyr Ile Ser Asp Ile Glu Phe Thr Asp Asn Ala His 30 10 Ile Leu Thr Ala Ser Gly Asp Met Thr Cys Ala Leu Trp Asp 25 35 (2) INFORMATION FOR SEQ ID NO:225: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 37 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

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- 266 -

(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: STE4-YEAST rIII, Fig. 44 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:225: Asp His Leu Gly Asp Val Leu Ala Leu Ala Ile Pro Glu Glu Pro Asn 5 10 Leu Glu Asn Ser Ser Asn Thr Phe Ala Ser Cys Gly Ser Asp Gly Tyr 10 20 25 Thr Tyr Ile Trp Asp 35 15 (2) INFORMATION FOR SEQ ID NO:226: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: STE4-YEAST rIV, Fig. 44 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:226: 35 Leu Asp Asn Gln Gly Val Val Ser Leu Asp Phe Ser Ala Ser Gly Arg 1.0 Leu Met Tyr Ser Cys Tyr Thr Asp Ile Gly Cys Val Val Trp Asp

(2) INFORMATION FOR SEQ ID NO:227:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

45 (B) TYPE: amino acid
(D) TOPOLOGY: unknown

- 267 -

(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 5 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: STE4-YEAST rV, Fig. 44 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:227: Gly His Gly Gly Arg Val Thr Gly Val Arg Ser Ser Pro Asp Gly Leu 5 10 15 Ala Val Cys Thr Gly Ser Trp Asp Ser Thr Met Lys Ile Trp Ser 20 25 30 (2) INFORMATION FOR SEQ ID NO:228: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rI, Fig. 45 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:228: Gly His Thr Gly Pro Val Tyr Arg Cys Ala Phe Ala Pro Glu Met Asn 10 40 Leu Leu Ser Cys Ser Glu Asp Ser Thr Ile Arg Leu Trp Ser 25

(2) INFORMATION FOR SEQ ID NO:229:

(i) SEQUENCE CHARACTERISTICS:

- 268 -

(A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rII, Fig. 45 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:229: Gly His Val Tyr Pro Val Trp Asp Val Arg Phe Ala Pro His Gly Tyr 5 10 20 Tyr Phe Val Ser Cys Ser Tyr Asp Lys Thr Ala Arg Leu Trp Ala 20 25 (2) INFORMATION FOR SEQ ID NO:230: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rIII, Fig. 45 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:230: Gly His Leu Ser Asp Val Asp Cys Val Gln Phe His Pro Asn Ser Asn 5 10

Tyr Val Ala Thr Gly Ser Ser Asp Arg Thr Val Arg Leu Trp Asp

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- 269 -

(2) INFORMATION FOR SEQ ID NO:231: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 5 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rIV, Fig. 45 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:231: Gly His Lys Gly Ser Val Ser Ser Leu Ala Phe Ser Ala Cys Gly Arg 20 5 10 Tyr Leu Ala Ser Gly Ser Val Asp His Asn Ile Ile Ile Trp Asp 20 25 25 (2) INFORMATION FOR SEQ ID NO:232: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 30 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 40 (C) INDIVIDUALLATE: TRNSCRPTION FCTR TIIF rV, Fig. 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:232: 45 Arg His Thr Ser Thr Val Thr Thr Ile Thr Phe Ser Arg Asp Gly Thr

15

- 270 -

Val Leu Ala Ala Ala Gly Leu Asp Asn Asn Leu Thr Leu Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:233: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 10 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 15 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 rI, Fig. 46 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:233: Ser Ser Asp Leu Tyr Ile Arg Ser Val Cys Phe Ser Pro Asp Gly Lys 5 10 25 Phe Leu Ala Thr Gly Ala Glu Asp Arg Leu Ile Arg Ile Trp Asp (2) INFORMATION FOR SEQ ID NO:234: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 35 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 40 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

45

(C) INDIVIDUAL ISOLATE: TUP1 rII, Fig. 46

- 271 -

Gly His Glu Gln Asp Ile Tyr Ser Leu Asp Tyr Phe Pro Ser Gly Asp
1 5 10 15

Lys Leu Val Ser Gly Ser Gly Asp Arg Thr Val Arg Ile Trp Asp
5 20 25 30

- (2) INFORMATION FOR SEQ ID NO:235:
 - (i) SEQUENCE CHARACTERISTICS:
- 10 (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

15

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 20 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 rIII, Fig. 46
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:235:

25

Ile Glu Asp Gly Val Thr Thr Val Ala Val Ser Pro Gly Asp Gly Lys

1 5 10 15

Tyr Ile Ala Ala Gly Ser Leu Asp Arg Ala Val Arg Val Trp Asp
30 25 30

- (2) INFORMATION FOR SEQ ID NO:236:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

PCT/US95/01210 WO 95/21252

- 272 -

(C) INDIVIDUAL ISOLATE: TUP1 rIV, Fig. 46 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:236: 5 Gly His Lys Asp Ser Val Tyr Ser Val Val Phe Thr Arg Asp Gly Gln 10 Ser Val Val Ser Gly Ser Leu Asp Arg Ser Val Lys Leu Trp Asn 20 10 (2) INFORMATION FOR SEQ ID NO:237: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 15 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 rV, Fig. 46 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:237: 30 Gly His Lys Asp Phe Val Leu Ser Val Ala Thr Thr Gln Asn Asp Glu 5 10 15 1 Tyr Ile Leu Ser Gly Ser Lys Asp Arg Gly Val Leu Phe Trp Asp 35 20 25 (2) INFORMATION FOR SEQ ID NO:238: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 amino acids 40 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 45

(iii) HYPOTHETICAL: NO

- 273 -

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rI, Fig. 47

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:238:

Asp Phe Ser Asp Asp Cys Arg Ile Ala Ala Ala Gly Phe Gln Asp Ser

10 1 5 10 15

Tyr Ile Lys Ile Trp Ser

- 15 (2) INFORMATION FOR SEQ ID NO:239:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid

20 (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rII, Fig. 47

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:239:

Gly His Ser Gly Thr Val Tyr Ser Thr Ser Phe Ser Pro Asp Asn Lys

1 5 10 15

Tyr Leu Leu Ser Gly Ser Glu Asp Lys Thr Val Arg Leu Trp Ser 20 25 30

- 40 (2) INFORMATION FOR SEQ ID NO:240:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

- 274 -

(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 5 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rIII, Fig. 47 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:240: Gly His Asn His Pro Val Trp Asp Val Ser Phe Ser Pro Leu Gly His 10 15 15 Tyr Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg Leu Trp Ser 25 20 30 20 (2) INFORMATION FOR SEQ ID NO:241: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rIV, Fig. 47 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:241: Gly His Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys 40 10 Tyr Val Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp

45

(2) INFORMATION FOR SEQ ID NO:242:

- 275 -

```
(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 31 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
10
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rV, Fig. 47
15
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:242:
          Gly His Thr Ala Pro Val Ile Ser Ile Ala Val Cys Pro Asp Gly Arg
                          5
                                              10
20
          Trp Leu Ser Thr Gly Ser Glu Asp Gly Ile Ile Asn Val Trp Asp
     (2) INFORMATION FOR SEQ ID NO:243:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 32 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
30
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
35
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rVI, Fig. 47
40
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:243:
          Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys Glu Gly
                      . 5
                                               10
45
          Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val Trp Asp
```

- 276 -

20 25 30

(2) INFORMATION FOR SEQ ID NO:244: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 10 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 15 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCU7 rI, Fig. 48 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:244: Gly His Phe Asp Ser Thr Asn Ser Leu Ala Tyr Ser Pro Asp Gly Ser 10 25 Arg Val Val Thr Ala Ser Glu Asp Gly Lys Ile Lys Val Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:245: 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 35 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 40 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:245:

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(C) INDIVIDUAL ISOLATE: YCU7 rII, Fig. 48

- 277 -

Glu His Thr Ser Ser Val Thr Ala Val Gln Phe Ala Lys Arg Gly Gln

1 5 10 15

Val Met Phe Ser Ser Leu Asp Gly Thr Val Arg Ala Trp Asp
5 20 25 30

- (2) INFORMATION FOR SEQ ID NO:246:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

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- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCU7 rIII, Fig. 48
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:246:

Arg Ile Gln Phe Asn Cys Leu Ala Val Asp Pro Ser Gly Glu Val Val 1 5 10 15

- Cys Ala Gly Ser Leu Asp Asn Phe Asp Ile His Val Trp Ser 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:247:
- 35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

PCT/US95/01210 WO 95/21252

- 278 -

(C) INDIVIDUAL ISOLATE: YCU7 rIV, Fig. 48

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:247: 5 Gly His Glu Gly Pro Val Ser Cys Leu Ser Phe Ser Gln Glu Asn Ser 10 Val Leu Ala Ser Ala Ser Trp Asp Lys Thr Ile Arg Ile Trp Ser 25 10 (2) INFORMATION FOR SEQ ID NO:248: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids 15 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 25 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rI, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:248: 30 Gly His Gly Ser Thr Ile Leu Cys Ser Ala Phe Ala Pro His Thr Ser 5 1 Ser Arg Met Val Thr Gly Ala Gly Asp Asn Thr Ala Arg Ile Trp Asp 20 25 35 (2) INFORMATION FOR SEQ ID NO:249:

(i) SEQUENCE CHARACTERISTICS: 40

(A) LENGTH: 31 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide 45

- 279 -

(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 5 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rII, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:249: 10 Gly His Tyr Asn Trp Val Leu Cys Val Ser Trp Ser Pro Asp Gly Glu 5 Val Ile Ala Thr Gly Ser Met Asp Asn Thr Ile Arg Leu Trp Asp 25 20 15 (2) INFORMATION FOR SEQ ID NO:250: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 38 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rIII, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:250: Gly His Ser Lys Trp Ile Thr Ser Leu Ser Trp Glu Pro Ile His Leu 35 Val Lys Pro Gly Ser Lys Pro Arg Leu Ala Ser Ser Ser Lys Asp Gly 20 40 Thr Ile Lys Ile Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:251:

(i) SEQUENCE CHARACTERISTICS:

- 280 -

(A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rIV, Fig. 49 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:251: Gly His Thr Asn Ser Val Ser Cys Val Lys Trp Gly Gly Gln Gly Leu 5 20 Leu Tyr Ser Gly Ser His Asp Arg Thr Val Arg Val Trp Asp 20 25 30 (2) INFORMATION FOR SEQ ID NO:252: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rV, Fig. 49 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:252: Lys Ile Cys Lys Lys Asn Gly Asn Ser Glu Glu Met Met Val Thr Ala 1 5

45 Ser Asp Asp Tyr Thr Met Phe Leu Trp Asn 20 25

- 281 -(2) INFORMATION FOR SEQ ID NO:253: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 amino acids (B) TYPE: amino acid 5 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVI, Fig. 49 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:253: Asn His Val Ala Phe Ser Pro Asp Gly Arg Tyr Ile Val Ser Ala Ser 20 10 Phe Asp Asn Ser Ile Lys Leu Trp Asp 20 25 (2) INFORMATION FOR SEQ ID NO:254: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 30 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 35 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 40 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVII, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:254:

Gly His Ile Ala Ser Val Tyr Gln Val Ala Trp Ser Ser Asp Cys Arg

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- 282 -

Leu Leu Val Ser Cys Ser Lys Asp Thr Thr Leu Lys Val Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:255:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 35 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

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- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVIII, Fig. 49
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:255:

Ser Val Asp Leu Pro Gly Ile Lys Thr Lys Leu Tyr Val Asp Trp Ser 1 5 10 15

Val Asp Gly Lys Arg Val Cys Ser Gly Gly Lys Asp Lys Met Val Arg
20 25 30

Leu Trp Thr

- 283 -

- (2) INFORMATION FOR SEQ ID NO:256:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: YKL525 rI, Fig. 50
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:256:
- Leu His Leu Tyr Ala Pro Val Phe Tyr Ser Asp Val Phe Arg Val Phe

 1 5 10 15

Met Glu His Ala Leu Asp Ile Leu Asp Ala Asn Trp Ser 20 25

25

- 284 -

- (2) INFORMATION FOR SEQ ID NO:257:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: YKL525 rII, Fig. 50
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:257:
- Val His Pro Asp Phe Val Thr Ser Ala Ile Phe Phe Pro Asn Asp Asp

 1 5 10 15

Arg Phe lle Ile Thr Gly Cys Leu Asp His Arg Cys Arg Leu Trp Ser 20 25 30

- 285 -

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rI, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:258:
- 20 Gly His Asn His Pro Val Trp Asp Val Ser Phe Ser Pro Leu Gly His
 1 5 10 15

Tyr Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg Leu Trp Ser 20 25 30

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- 286 -

(2)	INFO	RMATION	FOR	SEQ	ID	NO:259:
	(i)	SEQUENC	CE CI	HARAC	TEI	RISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

10 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rII, Fig. 51

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:259:

20 Gly His Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys
1 5 10 15

Tyr Val Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp
20 25 30

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- 287 -

(2) INFO	RMATION FOR SEQ ID NO:260:
(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown
(ii)	MOLECULE TYPE: peptide
(iii)	HYPOTHETICAL: NO
(iv)	ANTI-SENSE: NO
(vi)	ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rIII, Fig. 51

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:260:

20 Gly His Thr Ala Pro Val Ile Ser Ile Ala Val Cys Pro Asp Gly Arg
1 5 5 10 10 15

Trp Leu Ser Thr Gly Ser Glu Asp Gly Ile Ile Asn Val Trp Asp
20 25 30

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- 288 -

- (2) INFORMATION FOR SEQ ID NO:261:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

5 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rIV, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:261:
- 20 Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys Glu Gly
 1 5 10 15

Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val Trp Asp 20 25 30

- 289 -

(2) INFORMATION FOR SEQ ID NO:262:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

10 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

15 (C) INDIVIDUAL ISOLATE: WD40 Consensus Sequence

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:262:

Gly His Ser Ala Ala Leu Ala Leu Ala Leu Ser Pro Asp Ala Ala 20 1 5 10 15

Ala Ala Ala Leu Ala Ser Gly Ala Arg Asp Ala Thr Leu Arg Leu Trp
20 25 30

25 Asp Leu

- 290 -

(2) INFORMATION FOR SEQ ID NO:263:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

15 (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: WRTAA peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:263:

20 Trp Arg Thr Ala Ala

- 291 -

- (2) INFORMATION FOR SEQ ID NO:264:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide

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- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: WRTAV peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:264:
- 20 Trp Arg Thr Ala Val

- (2) INFORMATION FOR SEQ ID NO:265:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 4 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
- 10

- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: WRTA peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:265:
- 20 Trp Arg Thr Ala

- 293 -

Claims

1. A polypeptide composition effective to alter the activity of a first protein, wherein the first protein interacts with a second protein, and the second protein contains at least one WD-40 region,

said polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

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- 2. The composition of claim 1, wherein said polypeptide inhibits interactions between the first protein and the second protein; and/or wherein said polypeptide is an agonist of the activity of the first protein; and/or wherein said polypeptide is an antagonist of the activity of the first protein.
- 3. The composition of claim 1 or 2, wherein said WD-40 region has an amino acid sequence derived from the group consisting of SEO ID NO:76-261.

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- 4. The composition of claim 3, wherein said WD-40 region has an amino acid sequence selected from the group consisting of SEQ ID NO:76-261.
- 25 5. The polypeptide composition of claim 1 wherein said polypeptide is coupled to a solid support.
 - 6. A method to bind selectively said first protein which method comprises contacting a sample putatively containing said first protein with the polypeptide composition of claim 5; and

removing any unbound components of the sample from said composition.

7. A method to assess the interaction of a first protein
35 with a polypeptide having a sequence the same as a sequence of the same
length contained in a WD-40 region of a second protein, which method
comprises

contacting a sample containing said first protein with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in the WD-40 region of the second protein, and observing any interaction of the first protein with said polypeptide composition.

8. A method to assess the ability of a candidate compound 45 to bind a first protein which method comprises contacting said first protein with a polypeptide composition which binds said first protein,

- 294 -

wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts with said first protein, in the presence and absence of said candidate compound; and

measuring the binding of said polypeptide in the presence and in the absence of said candidate,

wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates that said candidate binds to said first protein.

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9. A method to alter the activity of a first protein that interacts with a second protein, where the second protein contains at least one WD-40 region, said method comprising

selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region in the second protein, and

contacting said polypeptide with said first protein under conditions which allow the formation of a complex between the polypeptide and the first protein, where said interaction is effective to alter the activity of the first protein.

- 10. The method of claim 9, wherein said contacting is effective to inhibit the interaction between said first and second proteins; and/or wherein said contacting is effective to stimulate the activity of said first protein; and/or wherein said contacting is effective to inhibit the activity of said first protein.
- 11. The method of any of claims 5-10, wherein said polypeptide is derived from the group consisting of SEQ ID NO:76-261.

- 12. The method of claim 11, wherein said polypeptide is selected from the group consisting of SEQ ID NO:76-261.
- 13. A composition of DNA molecules which consists of DNA molecules having a nucleotide sequence encoding the polypeptide of any of claims 1-4.
- 14. A DNA molecule which comprises an expression system for the production of the polypeptide of any of claims 1-4 which expression system comprises a nucleotide sequence encoding said polypeptide operably linked to control sequences capable of effecting the expression of said encoding nucleotide sequence.
- 15. Recombinant host cells modified to contain the 45 expression system of claim 14.

- 295 -

16. A method to produce a polypeptide having between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in a WD-40 region of a second protein which interacts with a first protein, which method comprises culturing the cells of claim 15 under conditions wherein said nucleotide sequence is expressed to produce said polypeptide; and

optionally recovering said polypeptide from the culture.

17. A polypeptide composition effective to alter the activity of a protein kinase C, where the protein kinase C interacts with a second protein, and the second protein contains at least one WD-40 region,

said polypeptide having between 4 and 50 amino whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

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- 18. The composition of claim 17, wherein said second protein is a receptor for activated protein kinase C.
- 20 19. The composition of claim 18, where said second protein has the sequence represented by SEQ ID NO:27.
 - 20. The composition of claim 17, wherein said polypeptide is an agonist of the activity of protein kinase C; and/or wherein said polypeptide is an antagonist of the activity of protein kinase C; and/or wherein said polypeptide inhibits interactions between protein kinase C and the second protein.
- 21. The composition of claim 20 wherein said polypeptide has the sequence represented by SEQ ID NO:7, SEQ ID NO:4 or SEQ ID NO:2.
 - 22. The composition of claim 17, wherein said WD-40 region has an amino acid sequence derived from the group consisting of SEQ ID NO:69-75.

23. The composition of claim 22, wherein said WD-40 region. has an amino acid sequence selected from the group consisting of SEQ ID NO:69-75.

- 24. The polypeptide composition of claim 17 wherein said polypeptide is coupled to a solid support.
- 25. A method to bind selectively protein kinase C which method comprises contacting a sample putatively containing protein kinase C with the polypeptide composition of claim 24; and

WO 95/21252

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removing any unbound components of the sample from said composition.

26. A method to assess the interaction of protein kinase C with a polypeptide having a sequence the same as a sequence of the same length contained in the WD-40 region of a second protein, which method comprises

contacting a sample containing said protein kinase C with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in the WD-40 region of the second protein, and observing any interaction of the protein kinase C with said polypeptide composition.

27. A method to assess the ability of a candidate compound to bind protein kinase C which method comprises contacting said protein kinase C with a polypeptide composition which binds said protein kinase C, wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts with said protein kinase C, in the presence and absence of said candidate compound; and

measuring the binding of said polypeptide in the presence and in the absence of said candidate,

wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates that said candidate binds to said protein kinase C.

28. A method to alter the activity of protein kinase C that interacts with a second protein, where the second protein contains at least one WD-40 region, comprising

selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region in the second protein, and

contacting said polypeptide with said protein kinase C under conditions which allow the formation of a complex between the polypeptide and the protein kinase C, where said interaction alters the activity of said protein kinase C.

29. The method of claim 28, wherein said contacting is effective to inhibit the interaction between said protein kinase C and said second protein; and/or wherein said contacting is effective to stimulate the activity of said protein kinase C; and/or wherein said contacting is effective to inhibit the activity of said protein kinase C.

- 297 -

- 30. The method of claim 29, wherein said polypeptide has an amino acid sequence represented by SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:7.
- 5 31. The method of claim 28, wherein said polypeptide is derived from the group consisting of SEQ ID NO:69-75.
 - 32. The method of claim 31, wherein said polypeptide is selected from the group consisting of SEQ ID NO:69-75.

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- 33. A composition of DNA molecules which consists of DNA molecules having a nucleotide sequence of encoding the polypeptide of any of claims 17-23.
- 15 34. A DNA molecule which comprises an expression system for the production of the polypeptide of any of claims 17-23 which expression system comprises a nucleotide sequence encoding said polypeptide operably linked to control sequences capable of effecting the expression of said encoding nucleotide sequence.

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- 35. Recombinant host cells modified to contain the expression system of claim 34.
- 36. A method to produce a polypeptide having between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in a WD-40 region of a second protein which interacts with protein kinase C, which method comprises culturing the cells of claim 35 under conditions wherein said nucleotide sequence is expressed to produce said polypeptide; and

30 optionally recovering said polypeptide from the culture.

CAAGGATGTG GAGTCATTCA CCTCTGTGCT GAAATAAACT TCCGGTGCCA GCAGTTCCCG **FGTTAGCGAT** AACCCTACGC AGACAAGACC GACCAACCAC **SCACCTITAC** CTACTGGCT(CATGGTAGAT GTGTACCTCT CGTCTCCTGC GACCCTTCGT ATGAAGGCAA GCCCCAACCG AGCCACCCCA **ATACCGACAA** CAGACTCTTA CCCTAAGCTA T666TCCC6 CCAGGATGA GCAAGCTAAA CAGATGGATC AGGGCAAGAT CCTGGGATGG **ACCCTATCAT TCGGCCACAC** CCGAGCAAAT CCACCACTCC **FGTGGAAGCT** ACTCCCACTI FGGGACTTGG AGCAAGGCAG **AAGTTTATGA** ACCATCATCA AGACGATTTG AAGTACACTG **AACAGCAGCA IGGGATCTCA** TGTGCTTCA TTTGCTGGCT ACTIGATICATION CTTCGAGGTC CTGGCTAACT GTGCTTGGCT ACACAGATCG CTCTCAGGCT CAGATTGTCT GGCTATGCTG CCAGACTCTG TACCCGCTAA GAACACAGTG CATCAATGCC TATCAAGATC CAGCACCAGC AAAAAAAAA CACTACCACG CAGCCGTGCG TCGAGACAAG CCAGTTTGCC GACAACCGG GGGTGTCTGC GGTGTGGAAT FGGATGGGTT CGCAACATCT ACAACGTGCT CTGGCCCCAG AAGAAGTTAT TGACTATTGG AAAAAAAAA GTGGAGACAT CTGCTGATGG **ACGGCATACC** CTTGTGTCCG AGGATGGCCA AGGGCCATAA CCTCTGATGG TCACAACGGG CTTTCTCCTC AGCTGGTCAA GTCGCGGTGG GTCGGCGTC GGAATACTCT CTGGCTATCT TGCGGCGACT GTATGGCAGG GGATGGGACA ATTGGCCACA **FCTGGAGGCA ACATTAGATG** TGTGCTGCCA GAACTGAAGC CTGAGCGTGG GGGACCCTCA CTCTGGGATC GGCACGAGGG GACATGATCC ATTAAGTTAT TCCTTGTCGC GAGACCAACT GTTGTCATCT SAATGGGTGT TGGCTTGGT 421 561 721 961 361 481 541 601 781 241 301

Fig. 1A

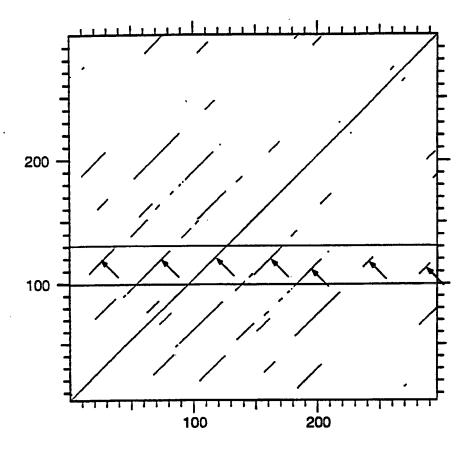


Fig. 1B

RACK 1	MTEQMTLRGTLKGHNGW <u>VTQ_IATT</u> PQFPDMILSASRDKTIIMWKLTRDETN(51)	Repeat I
	YGIPQRALR GHSHFVS DVVISSD GQFALSGSWDGTLRLWDLT(93)	RepeatlI
	TGTTTRRFVGHTKDVL SVAESSDNRQIVSGSRDKTIKLWNTLG(136)	RepeatIII
	VCKYTVQDESHSEW <u>VSCVRFS</u> PNSSNPIIVSCGWDKLVKVWNLA ₍₁₈₀₎	Repeat IV
	NCKLKTNHIGHTGYLN TVTV8PDGSLCASGCKDGQAMLWDL (221)	RepeatV
	NEGKHLYTLDGGDII NALCESPNRYWLCAATGPSIKIWDLEGKIIVDE (269) RepeatVI	RepeatVI
	LKQEVISTSSKAEP <u>PQCTSLA</u> WBADGQTLFAGYTDNLVRVWQVTIGTR(317)	RepeatVII

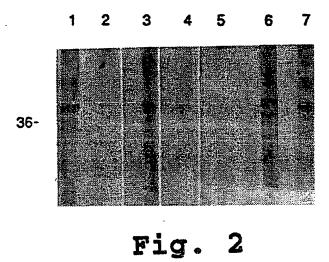
Rat

Fig. 10

GHS--V---V--SSD---ILSG--D-TIKLW-L GH---I---SVA---DG--LVTGS-D--C-IWDL

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Consensus sequence of repeats: Rat RACK1 Human Gp2



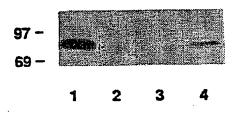
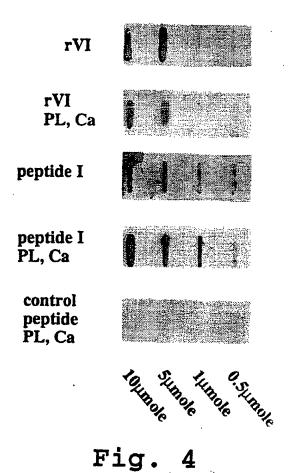
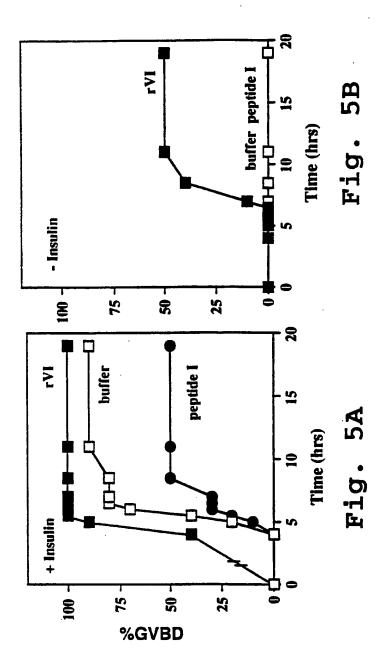
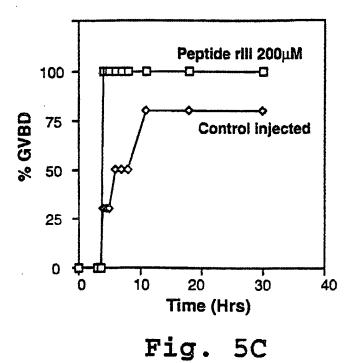


Fig. 3







pc pcpc pc

| 1 2 | 3 4 | 5 6 | 7 8 |

Peptide - rVI - I Insulin - - + +

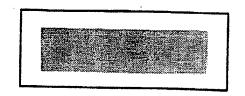
bPKC

Fig. 6

8 / 53

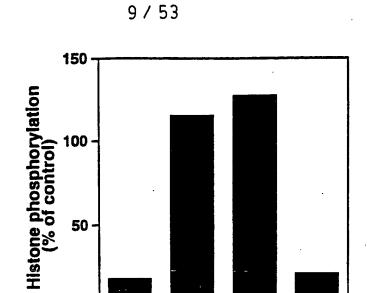
80- 78-	& KW	2	SAME SAME	4: - 3	# West	983 184	÷	-	A Per	128 CONTRACTOR OF THE PARTY OF
	1	2	3	4	5	6	7	8	9	
Arg-c	•	+	+	+	+	+	+	+	+	
PS(mg)	-	50	50	2.5	2.5	2.5	2.5	2.5	2.5	
DG (0.8 μg)	-	+	-	•	-	•	-	-	-	
Ca (mM)	-	1000	1000	50	50	50	50	50	50	
Peptide (10mM)	-	-	•	•	rVI	rVI	rVi	С	I	
Time of incubation (min)	30	30	30	30	5	15	30	30 .	30	

Fig. 7



	1	2	3	4	5	6
PS/DG/Ca	+	-	•	-	•	•
EGTA	-	+	-		•	•
Anti-pseudo- substrate antibodies	-	-	+	•	-	•
peptides (10mM)	-	•.		·rVI	I	С

Fig. 8



PS/DG/Ca - - + Peptide(10 mM) - rVI rVI I

Fig. 9

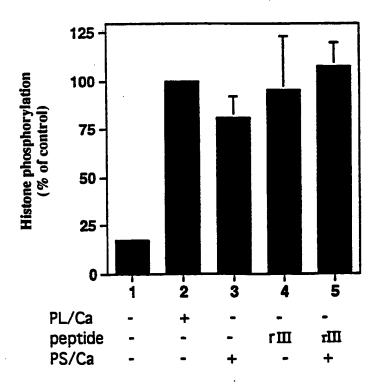


Fig. 10

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10 / 53.

Fig. 11

Human 56 kDa protein (PWP homolog)

1 mnrsrqvtcv awvrcgvake tpdkvelske evkrliaeak eklqeegggs
51 deeetgspse dgmqsartqa rprepledgd peddrtlddd elaeydldky
101 deegdpdaet lgesllgltv ygsndqdpyv tlkdteqyer edflikpsdn
151 livcgraeqd qcnlevhvyn qeedsfyvhh dillsaypls vewlnfdpsp
201 ddstgnyiav gnmtpvievw dldivdslep vftlgsklsk kkkkkgkkss

251 saeghtdavldlswnkl irnvlasasadntvil<u>wd</u>mslgk

291 paaslavhtd kvqtlqfhpf eaqtlisgsy dksvalydcr
331 spdeshrmwr fsgqiervtw 351 nhfspchfla stddgfvynl darsdkpift

381 lna<u>h</u>ndeisgldlssqi kgclvtasa<u>d</u>kyvki<u>wd</u>ilgdrp 421 slv<u>h</u>srdmkmgvlfcssccpdlpfiyafggqk<u>egl rvwd</u>i

461 stvssvneaf grrerlvlgs arnssisgpf gsrssdtpme 501 s

AAC-RICH protein

gsa <u>d</u> sivs <u>lwdiedm</u>	iycmefdptg kylaa	301 lpkstthvkhlktlyghtas iycmefdptg kylaaysa <u>d</u> sivs lwdi edm	301
ge <u>e</u> lnqvg <u>wd</u> nngdlilmansmgniea	vrwspdgdħlalidlptiktlkiykfn	vrwspdgdhla	235
elk <u>gh</u> dgsiekiswspknndlla s <mark>agtd</mark> kvik iwdv kigkcigtvstnseni	iekiswspknndlla s	elk <u>gh</u> dgs	182
	sknnniketi	plgnsnnnnnsnntss nsknnniketi	155
ssgs <u>dg</u> ivrv wn fd	<u>gn</u> kkkstsvawnangtkia s	gnkk	122
kestni pktntqytnf	gatgahlata gylasqihaq saqsalsnnl nsnskestni pktntaytnf dsknldlasr yfsecstkdfi	qatqqhlqtq qylqsqihqq dsknldlasr yfsecstkdfi	51
.hnqlhq qhnqqiqqqa	pggfqhlqqq qqqqqqqq qqqqqqqtq vqqlhnqlhq qhnqqiqqqa	pggfqhlqqq qqqqqqq	Н

351 mcvktfikst fpcrsvsfsf dgqfiaassf estieifhie 411 ssqpihtiecgvsslmwhptlpllayapesinennkdpsi rvfgyhs

Fig. 12

BETA TRCP

1 megfscslqp ptaseredcn rdepprkiit ekntlrqtklangtssmivp 51 kqrklsanye kekelcvkyf eqwsecdqve fvehlisrmchyqhghinty 101 lkpmlqrdfi talpargldh iaenilsyld akslcsaelv ckewyrvtsd 151 gmlwkklier mvrtdslwrg laerrgwgqy lfknkppdgk tppnsfyral 201 ypkiiqdiet iesnwrcgr

220	hslqr <u>ih</u> cr	se tskgvyclqyddql	ivsglr <u>d</u> n <u>tikiwd</u> kn tleckrv
268	lm <u>gh</u> tg	svlclqy dei	viitgs <u>d</u> s <u>tvrvwdv</u> ntgem
305	lntl <u>ih</u> hce	avlhlrfnngmmvtcsi	<u>d</u> r <u>s</u> ia <u>vwdm</u> asatditlrrv
351	lv <u>ah</u> raa	vnv vdfddkyivs	asg <u>d</u> r <u>tikvwn</u> tstcefvrt
391	ln gh krg	laclqyrdrlvvs	gss <u>d</u> n <u>tirlwdi</u> ecga
427	clrv le <u>gh</u> eel	vrc irfdnkrivs	gay <u>dg</u> k <u>ikvwdl</u> vaaldprapagt
475	lclrtlve <u>h</u> sgr	yfrl qfdefqi	vssshd <u>d</u> t <u>i</u> l <u>iwdf</u> lndpgla

Fig. 13

beta-prime-cop

vks vdlhptepwmlaslyngsvcvwnhetqtlv 51 ktfevcdlpv raakfvarkn wvvtgaddmqirvfnyntle

91	rvhmfe <u>ah</u> sdy	irciavhptqp	1	filtssd <u>d</u> mli <u>klwdw</u> dkkwscsq
137	vfe gh thy	vmqivinpkdnno	fa	s asl <u>d</u> r <u>tikvwal</u> gssspnft
181	l e gh ekg	vncidyysggdkp	yl	isgad <u>d</u> rl <u>vkiwd</u> yqnkt
221	cvqtle gh aq	nvscasfhpe	lp	iiitgse <u>dgtvriwh</u> sst
		·		

```
262 yrlestlnyg mervwcvasl rgsnnvalgy degsiivklgreepamsmda
318 ngkiiwakhs evqqanlkam gdaeikdger lplavkdmgs
351 ceiypqtiqh npngrfvvvc gdgeyiiyta malrnksfgs aqefawahds
401 seyairesns vvkifknfke kksfkpdfga esiyggfllg vrsvnglafy
451 dwentelirr ieiqpkhifw sdsgelvcia teesffilky lsekvlaaqe
501 thegvtedgi edgfevlgei qeivktglwv gdcfiytssv nrlnyyvgge
551 ivtiahldrt myllgyipkd nrlylgdkel nivsysllvs vleyqtavmr
601 rdfsmadkvl ptipkeqrtr vahflekqgf kqqaltvstd pehrfelalq
651 lgelkiayql aveaeseqkwkqlaelaisk cpfglaqecl hhaqdyggll
701 llatasgnas mvnklaegae rdgknnvafm syflqgklda clellirtgr
751 lpeaaflart ylpsqvsrvv klwrenlskv nqkaaeslad pteyenlfpg
801 lkeafvveew vkethadlwp akqyplvtpn eernvmeeak gfqpsrsaaq
851 qeldgkpasp tpvivtsqta nkeeksllel evdldnleie didttdinld
901 edildd
```

Fig. 14

CDC4 / CDC20 protein

```
1 mgsfplaefp lrdipvpysy rvsggiassg svtalvtaag thrnsstakt
51 vetedgeedi deyarkraag sgestpersd fkrvkhdnhk tlhpvnlant
101 gaasvdndgl hnltdisnda ekllmsvddg saapstlsvn mgvashnvaa
151 pttvnaatit gsdvsnnvns atinnpmeeg alplsptass pgtttplakt
201 tktinnnnni adlieskdsi ispeylsdei fsainnnlph ayfknllfrl
251 vanmdrsels digtlikdni krdlitslpf eislkifnyl afediinslg
301 vsqnwnkiir kstslwkkll isenfvspkg fnslnlklsq kypklsqqdr
351 lrlsflenif ilknwynpkf
371
                vpqrttlr<u>ah</u> mtsvitclqf
                                               ednyvitgaddkmirvvdsi
               nkkfllqls<u>ah</u>dggvwalkyahg
411
                                                 gilvsgstdr<u>tvrvwd</u>i
             kkgccthvfe <a href="mailto:ghnstvrcld">ghnstvrcld</a> iveyknikyi <a href="mailto:vtgsrdntlhvwklpkessvpdhgeehdyp">ttgsrdntlhvwklpkessvpdhgeehdyp</a>
451
511 lvfhtpeenp yfvgvlrghmasvrtvsghg
                                                 niv\sgsydntlivwdvaqm
                 kclyils<u>ah</u>tdriystiydh
561
erkrcisasm<u>d</u>t<u>tiriwdl</u>eniwnn<u>d</u>ecsyatnsasp
          cak ilgamytlq<u>ah</u>ta<del>lvgllrl----sdkfl</del>vsaaa<u>dg</u>s<u>irawd</u>an
618
```

```
661 dysrkfsyhh tnlsaittfy vsdnilvsgs enqfniynlr
701 sgklvhanil kdadqiwsvn fkgktlvaav ekdgqsflei ldfskaskin
751 yvsnpvnsss sslesistsl gltrttiip
```

Fig. 15

GBLP -CHLAMIDOMONAS HOMOLOG

1 maetltlratlkghtnwvtaiatpldpssntllsasrdksvlvwelerse
51 snygyarkalrghshfvadvvi ssdgqfcltgswdgtlrlwdlntgttr
101 rfvghtkdvlsvafs vdnrqivsgsrdktiklwntlgeck
141 ytigepeghtewyscvrfspmttnpiivsggwdkmvkvwnlt
183 ncklknnlvghhgyvntvtv spdgslcasggkdgiamlwdlaegkrly
231 sldagdvihclcfspnryw lcaatqssik wdlesksivddl
273 rpefnitskkaqvpycvslawsadgstlysgytdgqirvwavghsl

Fig. 16

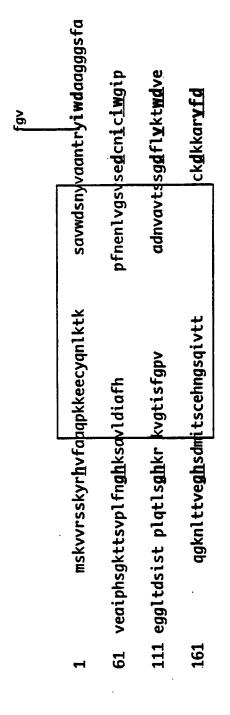
cop-1 protein

1 meeistdpvv pavkpdprts svgeganrhe nddggsggse igapdldkdl 51 lcpicmqiik dafltacghs fcymciithl rnksdcpccs qhltnnqlyp 101 nflldkllkk tsarhvskta spldqfreal qrgcdvsike vdnlltllae 151 rkrkmeqeea ernmqilldf lhclrkqkvd elnevqtdlq yikedinave 201 rhridlyrar drysvklrml gddpstrnaw pheknqigfn snslsirggn 251 fvgnyqnkkv egkaqgsshg lpkkdalsgs dsqslnqstv smarkkriha 301 qfndlqecyl qkrrqladqp nskqendksv vrregysngl adfqsvlttf 351 trysrlrvia eirhgdifhs anivssiefd rddelfatagvsrcikvfdf

- 401 ssvvnepadmqcpivemstrsklsqlswnk heknhliassdyegivtvwdv
- 451 ttrqslmeteenekraws<u>v</u>dfsrte psmlvs<u>as</u>d<u>d</u>c k<u>vkvw</u>ctrqeasvi
- 501 nidmkanicc vkynpgssny iavgsadhhi
- 531 hyydlrnisqplhvfs<u>ah</u>kka<u>v</u>symkflsnnelas<u>dst d</u>s t<u>lrlwdv</u>
- 551 kdn lpvrtfrght neknfvgltvnseylacgse
- 601 ttryvyhkei trpvtshrfg spdmddaekr qvptllvrfa
- 651 grvivprc

Fig. 17

CORO PROTEIN



pisfrvprks pktvslaggf vkkasavefk prtnsivnev vchagvknsr aifakdkvit vgfsktsere lhiydpraft tplsaqvvds asgllmpfyd adnsilylag kgdgniryye lvdespyihf keltn glkvtpftve pvvqvqegpk nekelreeye klkirvayle seivkkdaki difqgdiypd tyagepslta eqmvsgtnae lsefksatpq rglcflpkrc Intseceiar 251 301 351 201

Fig. 18

Coronin (p55)

- 1 mskvvrsskyrhvfaaqpkkeecyqnlkvtksawdsnyvaantryfgv<u>iwd</u>aagggsfav
 - 61 ipheasgkttsvplfn**gh**ksdvldiafhpfnenlvgsvse**d**cnic<u>iw</u>gipeggltdsist

 121 plqtls**gh**krkvgtisfgpvadnvavtssg**d**flv**k**t**wd**ve

 161 qgknlttve**gh**sdmitscewn hngsqivttck**d**kka<u>rvfd</u>prtnsivnev
 - 211 vchqgvknsr aifakdkvit vgfsktsere lhiydpraft
 251 tplsaqvvds asgllmpfyd adnsilylag kgdgniryye lvdespyihf
 301 lsefksatpq rglcflpkrc lntseceiar glkvtpftve pisfrvprks
 351 difqgdiypd tyagepslta eqwvsgtnae pktvslaggf vkkasavefk
 401 pvvqvqegpk nekelreeye klkirvayle seivkkdaki keltn

Fig. 19

CSTF 50kDa

- 1 myrtkvglkd raqlykliis allydgyisi anglineikp asvcapseal
- 51 lhliklgmen ddtavqyaig rsdtvapgtg idlefdadvq tmspeaseye
- 101 tcyvtshkgp crvatysrdg qliatgsada sikildterm laksampiev
- 151 mmnetaganm
- 201 enhpvirtly<u>dh</u>vdevtclafhpte qilasgsr<u>d</u>ytlk<u>lfd</u>yskpsakra

210 fkyigeaeml rsisfhpsgd filvgtqhpt lrlydintfqcfvsc

npqdahtdaicsvnyns sanmyvtaskdgciklwdgvsnrcittf

npqdahtdaicsvnyns sanmyvtaskdgciklwdgvsnrcittf

ekahdgaevcsaifsknskyilssgkdsvaklweistgrtlvrytgagls

grqvhrtqavfnhte dyvllpdertislccwdsrtaerrn

llslahnnivrcivh sptnpgfmtcsddfrarfwyrrstt d

Fig. 20

G-Beta 1 bovine

1 mseldqlrqe aeqlknqird arkacadatl sqitnnidpv griqmrtrrt

85 yttnkvhaiplrsswvmtcayapsgnyvacggldnicsiynlktregnvrvsrela

```
ghtgylsccrfldd nqivtssgdttcalwdietg

174 qqtttftghtgdvmslslap dtrlfvsgacdasaklwdvregmcrq

221 tftghesdin aicffpngna fatgsddatcrlfdlradqe

261 lmtyshdni cgitsvsfsksgrlllagyddfncnvwdal kadrag

307 vlaghdnrvsclg vtddgmavatgswdsflkiwn
```

Fig. 21

G-Beta- bovine (2)

1 rnqirdarka cgdstltqit agldpvgriq

31 mrtrrtlrghlakiyamhwgtdsr llvsasqdgkli<u>iwd</u>s

71 egnvryttnkvhaiplrsswvmtcayapsgnfvacggldnicsiyslktr

121	vsrelp <u>gh</u> tg	ylsccrfldd	nqiits	sg <u>d</u> ttca <u>lwd</u> ietg
161	qqtvgfa <u>gh</u> sg	dvmslslap	dgrtfvsg	ac <u>d</u> asik <u>lwd</u> vr
201	dsmcrqtfi gh es	dinavaffp	ngyafttg	sd <u>d</u> atcrl <u>fd</u> lradq
246	ellmy <u>sh</u> dn	iicgitsvaf	srsgrlllag	yd <u>d</u> fncn <u>iwd</u> amkgdr
291	agvla <u>gh</u> dn	rvsclgvt	ddgmavatg	sw <u>d</u> sflk <u>iwn</u>

Fig. 22

22/53

G- BETA DROSOPH

1 mneldslrqe aeslknaird arkaacdtsllqaatslepigriqmrtrrt

91 haiplrsswvmtcayapsgsyvacggldnmcsiynlktregnvr

```
vsrelpghggylsccrfl ddnqivtssgdmscglwdietglqv
tsflghtgdvmalsla pqcktfvsgacdasaklwdiregvckq
tfpghesdinavtf fpngqafqtgsddatcrlfdiradqe
lamyshdniicgitsvafsksgrlllagyddfncnywdtm
and kaersgilaghdnrvsclg vtengmavdtgswdsflrvwn
```

Fig. 23

G-BETA HUMAN

	_			•
1 mted	µmtlrgtlk gh ng	wvtqiattp	qfpdmil	sasr <u>d</u> k <u>ti</u> i <u>mwkl</u> trdet
51 nyg	jipqralr <u>gh</u> sh	fvsdvvi	ssdgqfal	sgsw <u>dgtlrlwdl</u> ttgtttrr
101	fv <u>ah</u> tk	dvlsvaf	ssdnrqiv	sgsr d k <u>tiklwn</u> tlgvcky
141	tvqde <u>sh</u> se	wvscvrfsp	nssnpiiv	scgw <u>d</u> klv <u>kvwnl</u> a nc
183	klktnhi gh tg	ylntvtv	spdgslca	sggk <u>dg</u> qam <u>l wdl</u>
222	negk <u>h</u> ly	tldggdiinald	cfspnrywl	caatgpsi <u>kiwdl</u> egkiivdel
271 kg	qevistsskaepp	actslawsad	gqtlf	agyt <u>d</u> nlv <u>rvwqv</u> tigtr

Fig. 24

G-Beta 2 (Human)

1 mseleqlrqe aeqlrnqird arkacgdstl tqitagldpv griqmrtrrt

51 lrghlakiya mhwgtds rllvsasqdgkli<u>iwd</u>syt

97 tnkvhaiplrsswvmtcayapsgnfvacggldnicsiyslktre

	1			•
151 .	gnvrvsrelp gh t	ylsccrfl	ddnqiitss	g <u>d</u> ttca <u>lwdi</u> etgqqtvgf
201	a <u>gh</u> s	dvmslslap	dgrtfvsgd	c <u>d</u> asik <u>lwdv</u> rdsmcrq
241	tfi <u>gh</u> e:	dinavaffpn	gyafttgs	d <u>d</u> atcr <u>lfd</u> lradqe
281	llmy <u>sh</u> dr	niicgitsvafsr	rsgrlllagy	d <u>d</u> fncn <u>iwd</u> am
321	kgdragvla gh di	rvsclgvtddgn	n avatgs	w <u>d</u> sflk <u>iwn</u>

Fig. 25

G-Beta 4 (mouse)

seleqlrqeaeqlrnqiqdarkacndatlvqitsnmdsv griqmrtrrt

```
51 lrghlakiyamhwgydsr llvsasqdgkli<u>iwd</u>syttnkm
```

91 haiplrsswvmtcayapsgnyvacggldnicsiynlktregdvrvsrela

```
ghtgylsccrflddg qiitssgdttcalwdietgqqtttf
tghsgdvmslslspd lktfvsgacdassklwdirdgmcrq
221 sftghisdinavsffpsg yafatgsddatcrlfdlradqe
261 lllyshdniicgitsvafsksgrlllagyddfncsvwdalkggrs
306 gvlaghdnrvsclgv tddgmavatgswdsflriwn
```

Fig. 26

GROUCHO PROTEIN DROSOPH

1 mypspvrhpa aggpppqgpi kftiadtler ikeefnflqa hyhsiklece
51 klsnektemq rhyvmyyems yglnvemhkq teiakrlntl inqllpflqa
101 dhqqqvlqav erakqvtmqe lnliigqqih aqqvpggppq pmgalnpfga
151 lgatmglphg pqgllnkppe hhrpdikptg legpaaaeer lrnsvspadr
201 ekyrtrspld iendskrrkd eklqedegek sdqdlvvdva nemeshsprp
251 ngehvsmevr dreslngerl ekpsssgikq erppsrsgss ssrstpslkt
301 kdmekpgtpg akartptpna aapapgvnpk qmmpqgpppa gypgapyqrp
351 adpyqrppsd paygrpppmp ydphahvrtn giphpsaltg gkpaysfhmn
401 gegslqpvpf ppdalvgvgi prharqintl shgevvcavt isnptkyvyt
451 ggkgcvkvwdisqpgnknpv sqldclqrdn yirsvkllpdgrtlivggea
501 snlsiwdlas

511	ptpri kael <u>ts</u> aa	pacyal aspd <u>skv</u> cfs	ccs <u>dgniavwdl</u>
553	hneilvrqfq <u>ah</u> td	gascidispdg <u>srl</u> wt	ggl d nt <u>v</u> rs <u>wdl</u> regrql

601 qqhdfssqif slgycptgdwlavgmenshv evlhaskpdk yqlhlhescv 651 lslrfaacgkwfvstgkdnl lnawrtpyga sifqsketss vlscdistdd 701 kyivtgsgdk katvyeviy

GTP binding protein (squid)

1 mtselealrqeteqlknqirearkaaadttlamatanvepvgriqmrtrr

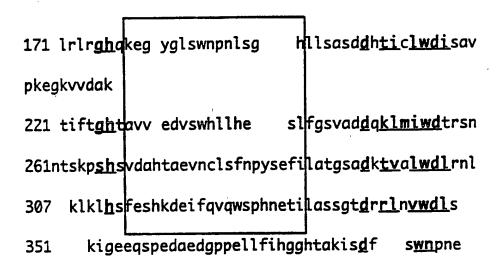
51 tlr<u>gh</u>lakiyamhwasd srnlvsqsq<u>d</u>gkliv<u>wd</u>gyttnk

91 vhaiplrssw vmtcayapsg nyvacggldn icsiyslktr egnvrvsrel

dnqivt\$sgdmtcalwnietgnqits gvtedgm<u>a</u>vatgs<u>wd</u>sflkiw n mrtfvsgacdasaklfdirdgick gfafat**g**sd<u>d</u>atcrl<u>fd</u>iradq 261 eigmy<u>sh</u>dniikgitsvafsksgrlllggyd<u>d</u>fncnv<u>wd</u>v 221 qtftghesdihaityfpn 181 fgghtgdvmslslapd 141 pghtgylsccrfid 301 lkqeragvla**gh**dnrvscl

IEF SSP 9306

1 madkeaafdd aveervinee ykiwkkntpf lydlvmthal ewpsltaqwl 51 pdvtrpegkd fsihrlvlgt htsdeqnhlv iasvqlpndd aqfdashyds 101 ekgefggfgs vsgkieieik inhegevnra rympqnpcii atktpssdvl 151 vfdytkhpsk pdpsgecnpd



387 pwvicsvsednimqvwqmelvldh

Fig. 29

HUMAN 12.3

1 1	mteqmtlrgtlk gh ng	wvtqiattpqfpdm	il	sasr <u>d</u> k <u>tiimwkl</u> trdet
51	nygipqralr <u>ghs</u> l	nfvsdvvissdgq	fal	sgsw <u>dgtlrlwdl</u> tt
95	gtttrrfv ght	k dvlsvafssdn	rqiv	sgsr d k tiklwn tlg
137	vcky tvqde <u>shs</u>	ewvscvrfspn	ssnpiiv	scgw <u>d</u> kl <u>ykvwnl</u> a
181	ncklktnhi <u>ght</u>	gylntvtvs	pdgslcd	sggk <u>dg</u> qam <u>lwdl</u> n
222	egk <u>h</u> ly	tldggdii nalc	spnrywl	caatgp <u>sikiwdl</u> e
263	gkiivdelkqevist	sskaeppqctslaws	adgqtlf	ngyt <u>d</u> nl <u>vrvwqv</u> tigtr

Fig. 30

IEF -7442 - human

1 maskemfedt veervineey kiwkkntpfl ydlvmthalq wpsltvqwlp 51 evtkpegkdy alhwlvlgth tsdeqnhlvv arvhipndda qfdashcdsd 101 kgefggfgsv tgkieceiki nhegevnrar ympqnphiia tktpssdvlv 151 fdytkhpakp dpsgecnpdl

171 rlr<u>ah</u>qkegyglswnsnlsghllsasd<u>d</u>htvcl<u>wd</u>inagpkegkivdaka
221ift<u>ah</u>savvedvawhllheslfgsvad<u>d</u>qklmi<u>wd</u>trsnt
261 tskpshlvda<u>h</u>taevnclsfnpysefilatgsa<u>d</u>ktval<u>wd</u>lrnlklklh
311 tfeshkdeifqv<u>h</u>wsphneti lassgt<u>d</u>rrlnv<u>wd</u>lskigeeqsaedaed
361 gppellfihg<u>ah</u>takisdfswnpnepwvicsvse<u>d</u>nimqi<u>wa</u>maeniynd

411 eesdvttsel egggs

insulin-like growth factor binding protein complex

1 malrkgglal allllswval gprslegadp gtpgeaegpa cpaacvcsyd

51 ddadelsvfc ssrnltrlpd gvpggtqalw ldgnnlssvp paafqnlssl

101 gflnlqggql gslepqallg lenlchlhle rnqlrslalg

141 tfahtpalasigisnnrisrledgifegigslwdlnigwn slavipdaaf rgigslrelv

201 lagnrlaylq palfsglael reldlsrnal raikanvfvq lprlqklyld
251 rnliaavapg aflglkalrw ldlshnrvag lledtfpgll glrvlrlshn
301 aiaslrprtf kdlhfleelq lghnrirqla ersfeglgql evltldhnql
351 qevkagaflg ltnvavmnls gnclrnlpeq vfrglgklhs lhlegsclgr
401 irphtftgls glrrlflkdn glvgieeqsl wglaelleld ltsnqlthlp
451 hrlfqglgkl eylllsrnrl aelpadalgp lqrafwldvs hnrlealpns

501 llaplgrlry lslrnnslrt ftpqppgler lwlegnpwdc gcplkalrdf 551 alqnpsavpr fvqaicegdd cqppaytynn itcasppevv gldlrdlsea 601 hfapc

Fig. 32

SUBSTITUTE SHEET (RULE 26)

insulin like growth factor binding protein complex - rat

1 malrtggpal vvllafwval gpchlqgtdp gasadaegpq cpvactcshd
51 dytdelsvfc ssknlthlpd dipvstralw ldgnnlssip saafqnlssl
101 dflnlqgswl rslepqallg lqnlyylhle rnrlrnlavg

141 lfthtpslaslslssnllgrleeglfaglshlwdlnlgwn

181 slvvlpdtvf qglgnlhelv

201 lagnkltylq palfcglgel reldlsrnal rsvkanvfvh lprlqklyld

251 rnlitavapg aflgmkalrw ldlshnrvag lmedtfpgll glhvlrlahn

301 aiaslrprtf kdlhfleelq lghnrirqlg ertfeglgql evltlndnqi

351 tevrvgafsg lfnvavmnls gnclrslper vfqgldklhs lhlehsclgh

401 vrlhtfagls glrrlflrdn sissieeqsl aglselleld lttnrlthlp

451 rqlfqglghl eylllsynql ttlsaevlgp lqrafwldis

491 hn<u>h</u>letlaeglfsslgrvrylslrnnslqtfspqpglerlwl<u>d</u>anp<u>wd</u>cs

541 cplkalrdfa lqnpgvvprf vqtvcegddc qpvytynnit cagpanvsgl dlrdvsethf

601 vhc

LIS1 (human)

- 1 mvlsgrgrde lnraiadylr sngyeeaysv fkkeaeldvn eeldkkyagl
- 51 lekkwtsvir lqkkvmeles klneakeeft sggplgqkrd pkewiprppe
- 101 kyals<u>ah</u>rspytrvifhpvfsvmvsase<u>d</u>atik<u>vwd</u>yetg

 151 dfertlk<u>ah</u>tdsyqdisfdhsgkllascsa<u>d</u>mtik<u>lwd</u>fqgfecir

 191 tmh<u>ah</u>dhnyssvaimpngdhivsasr<u>d</u>ktikm<u>wev</u>qtgycvktf

 241 t<u>ah</u>rewyrmyrpnqdgtliascsn<u>d</u>qtvr<u>yw</u>vvatkecka
- 291 elrehehvveciswapessy
- 311 ssiseat**gs**etkksgkpgp fllsgsr**d**kt km<u>wdv</u>stgmc 351 lmtlv**gh**dnwyrgvlfhsggkfilscad**d**ktlr<u>vwd</u>yknk 391 rcmktlna**h**ehfytsldfhktapyvvtgsv**d**qtvk<u>vwe</u>cr

Fig. 34

MD6

1 merkdfetwl dnisvtflsl mdlqknetld hlislsgavq lrhlsnnlet 51 llkrdflkll plelsfyllk wldpqtlltc clvskqrnkv isactevwqt 101 acknlgwqid dsvqdslhwk kvylkailrm kqledheafe

				1
141	tssli gh s	rvyalyyk	dgllct	gsd <u>d</u> l <u>s</u> a <u>klwdvstgqc</u>
181	vygiqt <u>h</u> to	a avkfde	qklvt	gsf <u>d</u> n <u>tv</u> ac <u>wew</u> ssgart
220	qhfr <u>gh</u> tg	avfsvdysdel	dilvs	gsa <u>d</u> fa <u>vkvw</u> a <u>l</u> sagtc
261	lntlt <u>gh</u> te	wvtkvvlqkckvksllhsp	gdyill	sa <u>d</u> k y ei <u>kiw</u> p <u>i</u> grei
]

301 nckclktlsv sedrsiclap rlhfdgkyiv cssalglyqw 351dfasydilrv iktpevanla llgfgdvfal lfdnhylyim dlrteslisr 401wplpeyrksk rgtsflager pg

Fig. 35

MSL1

1 mnqcakdith eassipidlq eryshwkknt kllydylntn stkwpsltcq
51 ffpdldttsd ehrillssft ssqkpedeti yiskistlgh ikwsslnnfd
101 mdemefkpen strfpskhlv ndisiffpng ecnrarylpq npdiiagass
151 dgaiyifdrt khgstrirqs kishpfetkl fgshgviqdv eamdtssadi
201 neatslawnl qqealllssh sngqvqvwdi kqyshenpii dlolvsinsd
251 gtavndvtwm pthdslfaac tegnavslld lrtkkeklqs

291 nrekhdggvnscrfn yknslilasadsngrlnlwdirnmn
331 kspiatmehgtsvstlewspnfdtvlatagaedgl vklwdtsceetifth
381 gahmlgvndisw dahdpwlmcsvandn svhiwkpagnlvg hs

MUS MUSCULUS PROTEIN

gggslfypye leagevveaq nvqnlfhrye leegevveaq vvqsmfpyye 101 sledsdnfis clensyipqn vengevveeq slgrrfhpye leagevvegq learevigaq ggqglsrhyg leggevveat eddslidewi 51 ssdvtgteds svltpqstdv nsvdsyqgye gddddeedde ddkdgdsnlp 1 msshesytna aetpenisil sclgetsgal vdtktisdik tmdprvsltp aletsplprp rwnvisalrd rqlgssgrfv yeacgarlfv qrfs 251 avrrlighhe leegedvddq eessemheet sedsseqydi leagevveae evqgffqrye 201 151

fnqhgt|lasgsddlkvivwdw</u>lkkrsvln

351 lehvfeghsgdvntvh

Fig. 37A

391 fdsghknnilgakflpncnd ailamcgrdg qvrvaglsav

401 agthmtkrlv khggashrlglepdspfrfl tsgedavvfn

451 idlrqahpas kilvikdgdk kvglytvfvn

panvyqfavg gqdqfmriyd qrkidenvnn gvlkkfcphh llssdypahi 501

tslmysydgt eilasynded iyifnssdsd gaqyakrykg hrnnstvkgv

01 yfygprsefv

611 msgsdca hifiweksscqiv qfleadeggt incidshpylpvldssgld h e vkimspiae

671 pskklaglkn vikinklkrd nftlrhtslf 701nnsmlcflms hvtqsnygrswrgirinagg gdfsdsssss eetnqes

Fig. 37B

ORF RB1

1 mnqcakdith eassipidlqeryshwkknt kllydylntn stkwpsltcq 51 ffpdldttsd ehrillssft ssqkpedeti yiskistlghikwsslnnfd 101 mdemefkpen strfpskhlv ndisiffpng ecnrarylpq npdiiagass 151 dgaiyifdrt khgstrirqs kishpfetkl fgshgviqdv eamdtssadi 201 neatslawnl qqealllssh sngqvqvwdi kqyshenpii dlplvsinsd 251 gtavndvtwm pthdslfaac tegnavslld lrtkkeklqs

```
nrekhdggvnscrfnykn slildsadsngrlnlwdirnmn
slildsadsngrlnlwdirnmn
kspiatmehgtsvstlewspnfdtvlatagqedg lyklwdtsceetifth
gahmlgvndiswdah dpwlmcsvandn syhiwkpagnlyghs
```

Fig. 38

Periodic Trp protein.

1 misatnwvpr gfssefpeky vlddeeveri nqlaqlnldd akatleeaeg
51 esgveddaat gssnklkdql didddlkeyn leeyddeeia dneggkdvsm
101 fpglsndsdv kfhegekged pyislpnqed sqeekqelqv ypsdnlvlaa
151 rteddvsyld iyvyddgagf hssdipveeg deadpdvarg lvrdpalyvh
201 hdlmlpafpl cvewldykvg snseeaanya aigtfdpqie iwnldcvdka
251 fpdmilgepl dnsmvslksk

271 kkkkkskt<u>gh</u> ittnhtdavl smahnkyfrsvlastsa<u>d</u>htv kl<u>wd</u>lnsgn 321 aarslasi<u>h</u>s nknvsssewhmlngsilltggydsrvaltdvris<u>d</u>esqmsky<u>w</u>samagee

- 381 ietvtfasen iilcgtdsgn vysfdirnne nrkpvwtlka
- 421 hdagistlcs nkfipgmmst gamgektvkl
- 451 wkfplddatn tkgpsmvlsr dfdvgnvlts sfapdievag tmviggvnkv
- 501 lklwdvftnr svrksfksel envqarakee aqkigkssri arkytsndnp 551 dtvitiddqg edeeereggd ehddma

PLAP

1 mhymsghsnf vsyvciipss diyphgliat ggndhnicif sldspmplyi

- 51 lkghkdtvcslssgkf gtllsgswdttakvwlndkcmmtl
 91 qghtaavwavkilpeqglmltgsadktiklwkagrcertf
 131 lghedcvrglails eteflscandasirrwaitgeclevy
 171 fghtmyiysisvfpnskdfvttaedrslriwkhgecaqti
- 211 rlpaqsiwcc cvlengdivv gasdgiirvf teseertasa
 251 eeikaslsre spliakvltt eppiitpvrr tlpcrvtrsm issclsrlvs
 301 tslstsdshl titalhlflt tttte

Fig. 40

RETINOBLASTOMA BINDING PROTEIN - HUMAN

1 madkeaafdd aveervinee ykiwkkntpf lydlvmthal ewpsltaqwl

51 pdvtrpegkd fsihrlvlgt htsdeqnhlv iasvqlpndd aqfdashyds

101 ekgefggfgs vsgkieieik inhegevnra rympqnpcii atktpssdvl

151 vfdytkhpsk pdpsgecnpd

lsghl∜sasd**d**hticl**md**isavpkegkvvdak 261 ntskp<u>sh</u>svdahtaevnclsfnpysefildtgsa<u>d</u>ktval**wd**lrnlklkl heslfgsvaddqklmi**wd**trsn 1r1rghqkegyglswnpn tiftghtavvjedvswhll 171 221

vidsvsednimqvwqmaeniyndedpegsvdpegqgs fihgghtakisdfswnpnepw 374

hsfe**sh**kdei|fqvqwsph

311

netildssgt**d**rrlnv**md**lskigeeqspedaedgppell

S253 PROTEIN

1 mfksktstls ydetpnsneg drnatpvnpk eksqtkhlni pgdrsrhssi 51 adskrsssry dggysadiip aqlrfidnid ygtrlrktlh rnsvvsngyn 101 klsendrwyf dlfdrkyfen yleeptyiki fkkkegleqf drmflaqelk 151 ipdvykstty qgepavanse lfknsiccct fshdgkymvi gckdgslhlw 201 kvinspvkrs emgrseksvs asranslkiq rhlasisshn gsissndlkp 251 sdqfegpskq lhlyapvfys

271 dvfrvfmehaldildanw skngflitasmdktaklwhper
 311 kyslktfvhpdfvtsaiffpnddrfiitgcldhrcrlwsi

351 ldnevsyafd ckdlitsltl sppggeytii gtfngyiyvl lthglkfvss
401 fhvsdkstag ttknsfhpss eygkvahgpr itglacffsk vdknlrlivt
451 tndskiaifd lnekkplelf kgfasgssrh rgaflmmkne pvvftgsddh
501 wfytwkmasf nlsaemncta phrkkrlsgs mslkgllriv snkstndecl
551 tetsnassh tftnssknvl atatvgsaai knnhyisfha hnspvtcasi
601 apdvaiknls lsndlifelt sayfkemgan ysesketcdn kpnhpvtetg
651 gfssnlsnvv nnvgtilitt dsaglirvfr tdilpeirkk iiekfheynl
701 fhleaagkin nhnndsilen rmderssted nefsttppsn thnsrpshdf
751 celhpnnspv isgmpsrasa ifknsifnks ngsfislksr sestsstvfg
801 phdiprvstt ypklkcdvcn gsnfecaskn piaggdsgft cadcgtilnn
851 fr

Fig. 42

S0F1

mkiktikrsa ddyvpvkstq esqmprnlnp elhpferare ytkalnatkl

aiaknygslnklatdsa<u>d</u>gviky<u>wn</u>mstr ermfakpfvgqlgy<u>ah</u>rddvy 2

eefvsfkahyglvt<u>gl</u>cv¶aprfhdkkpdlksqnfmlsdsd<u>d</u>ktvk<u>lws</u>invddysnkns

101

161

sdndsvtnee**gl**irlfdgesafqgidshrenstfdtg**g**akihl**wd**vnrlk

pvsdlswgad nitslkfnqn etdilastgs dnsivlydlr tnsptqkivq tmrtnaicwn 211

pmeafnfvta nedhnayyyd mrnlsrslnv fkdhvsavmd vdfsptgdei vtgsydksir 271

iyktnh**gh**sreiyhtkrmqhvf vkysmdskyiisgsd<u>dg</u>nvr<u>l**wr**skaw</u>

331

ersnvkttre knkleydekl kerfrhmpei krisrhrhvp qvikkaqeik 381

nielssikrr eanerrtrkdmpyiserkką ivgtvhkyed sgrdrkrrke ddkrdtqek 431

STE4 - YEAST

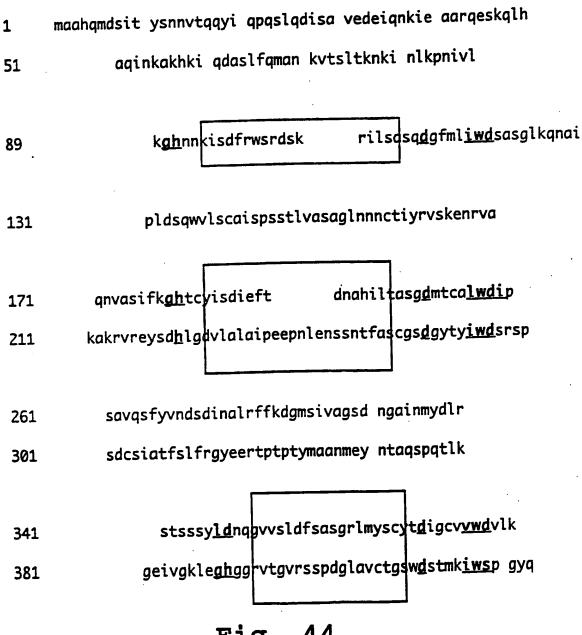


Fig. 44

TRANSCRIPTION FACTOR TIIF

hlgeakrqdn kmrvyygllk evdfqtlttp apapeeeddd pdapdrpkkk kpkkdpllsk ksksdpnaps idriplpelk dsdkllklka ldiykhelsm vlypilvqiy cdldgyyieg lfnllllskp eellendlvv msrdshslfk rhiqdrrqev vadivskylh fdtyegmarn 51 velseisesd vaqvlgavlg agdanrerkh vaspaqghkq savteanaae 1 mslevsning gngtqlshdk rellcllkli kkyqlkstee llcqeanvss fdaqhyeqay kelrtfveds skdqlpsavfytvln fkilasglre kakefiekyk ameqdkfvir klqcvatags elakfiddds **lreaskrlal** 101 151 301 201 251

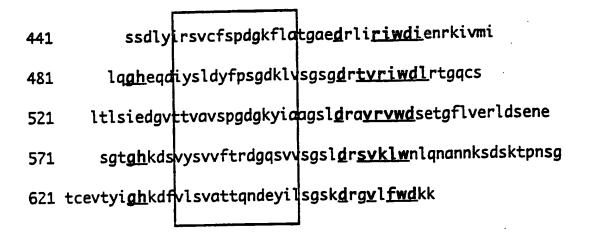
Fig. 45A

lreldkesadi shqgvtcaeisddstm lacgfg<u>d</u>ssv<u>riw</u>sltpanvrtlkdads twscvvtyr<u>ah</u>vypvwdvrfaphgyyfyscsy<u>dkta<u>rlw</u>atdsnqalrvf</u> vghlqdvdcvqfhpnsnyvdtgss<u>drtvrlmd</u>nmtgqsvr lmtghkdsvsslafsacgryldsgsvdhnii**imd**lsngsl 651 tedyisnhit vshhqdende^Ldvylmrtfps knspfvslhf trrnllmcvg 701 lfks vttllrhtstvttitfsrdgtvldaagldnn1tlmd£hkv 431 nvrmlddrsgevtrslmghtdpvyrcafapemnll¶scse<u>dstirlW</u>sll 376 571 481 531 611

rig. 45B

TUP1

1 mtasvsntqn klnelldair qeflqvsqea ntyrlqnqkd ydfkmnqqla 51 emqqirntvy elelthrkmk dayeaeikhl klgleqrdhq iasltvqqqq 101 qqqqqqqq hlqqqqqla aasasvpvaq qppattsata tpaantttgs 151 psafpvqasr pnlvgsqlpt ttlpvvssna qqqlpqqqlq qqqlqqqpp 201 pqvsvaplsn taingsptsk etttlpsvka pestlketep ennntskind 251 tgsattattt tateteikpk eedatraslh qdhylvpynq ranhskpipp 301 flldldsqsv pdalkkqtnd yyilynpalp reidvelhks ldhtsvvccv 351 kfsndgeyla tgcnkttqvy rvsdgslvar lsddsaannh rnsitenntt 401 tstdnntmtt tttttitta mtsaaelakd venlntsssp



661 sgnpllmlqg hrnsvisvav angsslgpey nvfatgsgdc 701 kariwkykki apn

Fig. 46

TUP1 HOMOLOG

msqkqstnqn qngthqpqpv knqrtnnaag ansgqqpqqq sqgqsqqqgr sqgfsqdqgr kgyhrteaml raesgrtltp qnkqspantk ppnpgktakp isnptnlssk rdaeggivss grleglnape nwiraysmlk nwidssleiy kpelsyimyp ifiylflnlv aknpvyarrf svnsidhike nevasafqsh kyritmsktt lnlllyflne nesiggslii svinqhldpn ivesvtarek ladgikvlsd sengngkqnl emnsvpvklg pfpkdeefvk eietelkikd dqekqlnqqt agdnysgann rtllqeykam nnekfkdntg dddkdkikdk iakdeekkes lplppktald lkleiqkvke srdaikldnl qlalpsvcmy

461	tfqntnkdmscldfsd	dcriaaag	fq <u>d</u> sy	i <u>kiw</u> s <u>l</u> dgsslnnpnialnnn
511	dkdedptcktlv <u>gh</u> sg	tvystsf spdnkyl	lsgse <u>d</u> k <u>t</u>	<u>vrlw</u> smdthtal
561	vsyk <u>gh</u> nh	pvwdvs fsplghyt	atash <u>d</u> qt	a <u>rlw</u> scdhiy
601	plrifa <u>gh</u> lr	dvdcvs fhpngcy	ftgss d k <u>t</u>	c <u>rmwdv</u> st
641	gdsvrlfl <u>ah</u> td	pvisi avcpdgrw	stgse <u>d</u> gi	<u>i</u> n <u>vwdi</u> gtgkr
686	1kqmr <u>ghg</u> l	naiyslsyskegnv	isgga <u>d</u> h <u>t</u>	<u>vrvwd</u> lkkattep

731 saepdepfig ylgdvtasin qdikeygrrr tviptsdlva 771 sfytkktpvf kvkfsrsnla laggafrp

Fig. 47

YCU7

1 mvrrfrgkel aattfnghrd yvmgaffshd qekiytvskd gavfvweftk 51 rpsddddnes edddkqeevd iskyswritk khffyanqak vkcvtfhpat 101 rllavgftsg efrlydlpdf tliqqlsmgq npvntvsvnq tgewlafgss 151 klgqllvyew

qsesyilkqqghfdstnslay spdgsrvvtasedgkikvwd
tsgfclatfeehtssvta vqfakrgqvmfsssldgtvrawdli
ryrnfrtftgteriqfnclavdpsgevvcagsldnfdih vwsvqt
gqlldalsghegpvscl sfsqensvlasaswdktiriwsi

341 fgrsqqvepi evysdvlals mrpdgkevav stlkgqisif niedakqvgn 391 idcrkdiisg rfnqdrftakilndpnfllq yitvlmvwll wlvviitpfv 431 ymmfqmksc

Fig. 48

YCW2 PROTEIN

1 mstlipppsk kqkkeaqlpr evaiipkdlp nvsikfqald tgdnvggalr 51 vpgaisekql eellnqlngt sddpvpytfs ctiqgkkasd pvktiditdn 101 lysslikpgy nstedqitll ytpravfkvk

131	pvtrsssaia <u>gh</u> gst	ilcsafaph	tssrmv	tgag <u>d</u> ntari <u>w</u> dcdtqtpmh
181	tlk <u>ah</u> ynw	vlcvswsp	dgevia	tgsm <u>d</u> ntirl <u>w</u> dpksgqc
221	lgdalr gh skw	itslswepihlvk	kpgskprla	sssk <u>d</u> gtiki <u>w</u> dtvsrvc
271	qytms <u>ah</u> tns	vscvkwggqg	lly	sgsh d rtvrv w dinsqg
			المالية المالي	

311 rcinilksha hwvnhlslst dyalrigafd htgkkpstpe

```
and a second sec
```

Fig. 49

Fig. 50

YKL525

1 mfksktstls ydetpnsneg drnatpvnpk eksqtkhlni pgdrsrhssi 51 adskrsssry dggysadiip aqlrfidnid ygtrlrktlh rnsvvsngyn 101 klsendrwyf dlfdrkyfen yleeptyiki fkkkegleqf drmflaqelk 151 ipdvykstty

161 qgepavanselfknsiccct fshdgkymvi gckdgslhlwk

202 vinspykrs emgrseksys asranslkiq rhlasisshn gsissndlkp

251 sdqfegpskql**h**lyapvfysdvf rvfmehal<u>d</u>ildan**w**skngflitasmd 301 ktaklwhperkyslktfv**h**pdfvtsaiffpnddrfiitgcl<u>d</u>hrcrl**w**si

351 ldnevsyafd ckdlitsltl sppggeytii gtfngyiyvl lthglkfvss
401 fhvsdkstqg ttknsfhpss eygkvqhgpr itglqcffsk vdknlrlivt
451 tndskiqifd lnekkplelf kgfqsgssrh rgqflmmkne pvvftgsddh
501 wfytwkmqsf nlsaemncta phrkkrlsgs mslkgllriv snkstndecl
551 tetsnqsssh tftnssknvl qtqtvgsqai knnhyisfha hnspvtcasi
601 apdvaiknls lsndlifelt sqyfkemgqn ysesketcdn kpnhpvtetg
651 gfssnlsnvv nnvgtilitt dsqglirvfr tdilpeirkk iiekfheynl
701 fhleaagkin nhnndsilen rmderssted nefsttppsn thnsrpshdf
751 celhpnnspv isgmpsrasa ifknsifnks ngsfislksr sestsstvfg
801 phdiprvstt ypklkcdvcn gsnfecaskn piaggdsgft cadcgtilnn
851 fr

yrb 1410 yeast

1 msqkqstnqn qngthqpqpv knqrtnnaag ansgqqpqqq sqgqsqqqgr
51 sngpfsasdl nrivleylnk kgyhrteaml raesgrtltp qnkqspantk
101 tgkfpeqssi ppnpgktakp isnptnlssk rdaeggivss grleglnape
151 nyiraysmlk nwvdssleiy kpelsyimyp ifiylflnlv aknpvyarrf
201 fdrfspdfkd fhgseinrlf svnsidhike nevasafqsh kyritmsktt
251 lnlllyflne nesiggslii svinqhldpn ivesvtarek ladgikvlsd
301 sengngkqnl emnsvpvklg pfpkdeefvk eietelkikd dqekqlnqqt
351 agdnysgann rtllqeykam nnekfkdntg dddkdkikdk iakdeekkes
401 elkvdgekkd snlsspardi lplppktald lkleiqkvke srdaikldnl
451 qlalpsvcmy tfqntnkdms cldfsddcri aaagfqdsyi kiwsldgssl
501 nnpnialnnn dkdedptckt lvghsgtvys tsfspdnkyl lsgsedktvr

Fig. 51A

551 lwsmdthtalvsykghnhpv vdvs fsplghyfatashdqtarlwscdhiy
601 plrifaghlndvdcvs fhpngcyvftgssdktcrmwdvst
641 gdsvrlflghtapvisiav cpdgrwlstgsedgiinvwdigtgkrlkqmr
691 ghgknaiyslsyskegnvlisggadhtvrvwdlkkattep
731 saepdepfig ylgdvtasinadikeyarrr tviptsdlva sfytkktpvf
kvkfsrsnla laggafrp

Fig. 51B